Heart Failure (HF)

- 5.8 million in US; 23 million worldwide
- Increasing: aging population; improved management of heart disease
- 5 year mortality: improving, but rivaling many cancers
- Major source of costs: $39 billion in US

AHA: Circulation 2010
Prevalence of CAD in Multicenter CHF Trials

24 consecutive heart failure trials in *N Engl J Med* since 1986
Total = 43,568
CAD = 26,877

62% CAD
38% Non-CAD

from Gheorghiade et al. *Circulation* 2006;114:202-213

Prevalence of CAD in Clinical Practice

ADHERE Registry – Patients with systolic dysfunction
Total = 47,000
CAD = 29,610

63% CAD
37% Non-CAD

from Fonarow et al. *J Card Fail* 2003;9:S79
Dysfunctional But Viable Myocardium: Relationship to Myocardial Perfusion

**Hibernating myocardium**
- Perfusion reduced at rest but adequate for tissue viability

**Repetitive stunning**
- Perfusion: normal at rest, decreased during minimal exertion

**Both states:**
- Critical stenoses
- Perfusion would worsen with exercise

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**Extent of Myocardial Viability**
**Potential Guide to Therapeutic Decisions**

- Extensive viable myocardium:
- Revascularization (PCI, CABG)
Assessment of Viable Myocardium

- SPECT (rest/redistribution thallium, NTG mibi/tetro)
- PET (FDG compared with SPECT/PET perfusion)
- MRI (delayed enhancement)
- Echo: Low-dose dobutamine

GARRUS 60 yo M with recent CP referred for stress testing
Rest TI-201 performed as part of dual isotope protocol
REST REDISTRIBUTION TI-201 PROTOCOL

REST TI-201
3.0-4.5mCi

GATED SPECT

* No CHO from 4 hrs before to 4 hrs after injection

** significant gain in viable segments reported - no reinjection

Infarct sizing and detection: DE MRI vs. SPECT
27% by DE-MRI, 31% by SPECT

Sizing: N=26, r =0.85
Detection: N=82, Sens =87%, Spec=91%

Slomka, Fieno, Thomson, et al JNM 2005
Quantitative TI-201 SPECT vs Quantitative CMR
For Myocardial Infarct Detection

ROC AUC = 0.91

Rest vs Redistribution TI-201 SPECT
for Infarct Size: Comparison with DE CMR

Fieno…Slomka, et al JNC 2007
**ARAJAC (90 M): HTN, SOB: no known CAD**

<table>
<thead>
<tr>
<th></th>
<th>SHORT AXIS</th>
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<th>VERTICAL LONG AXIS</th>
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<th>HORIZONTAL LONG AXIS</th>
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<td>BASAL</td>
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<td><img src="image15.jpg" alt="Image" /></td>
</tr>
</tbody>
</table>
ARAJAC (90 M): HTN, SOB: no known CAD

NTG-sestamibi for myocardial viability

Accuracy of AC Nitrate Augmented Tc-99m Tetrofosmin in Predicting FDG PET

54 pt with LV dysfunction; PET changed management by finding >20% viable myocardium not ID by Tc-99m

Rana et al JNC 2012
SPECT-MPI and PET-FDG for Viability Assessment

Strengths:
• Both well validated, standardized, quantitative
• PET
  • Likely more accurate than PET
  • Widely available (all centers that offer FDG-PET and SPECT-MPI)

Limitations
• Limited resolution does not allow for quantitation of the transmural extent of scar

Dobutamine Echo: Biphasic Response
Low-dose Dobutamine Echo

- Widely available, easily performed
- Highly specific
- Specificity even higher with bi-phasic response
- Subjective, non-quantitative

Delayed Hyperenhancement on ceCMR
Distinction Between Reversible and Irreversible Injury

Predicting Recovery of Function

MRI Hyperenhancement


Images in Cardiovascular Medicine

Reversible Wall Thinning in Hibernation Predicted by Cardiovascular Magnetic Resonance

Anna S. John, MB, MRCP; Gilles D. Dreyfus, FRCS; Dudley J. Pennell, MD, FRCP

Paradigm shift away from acceptance of severe wall thinning as predictive of non-viability?

Causes of Delayed Enhancement other than Myocardial Infarction

– Chagas’ Disease (Rochitte, JACC, 2005)
– Myocarditis (Mahrholdt, Circ, 2004)
– Hypertrophic obstructive cardiomyopathy (Kim, JACC, 2002)
– Sarcoidosis (Kanao, JCAT 2005)
– Amyloidosis (Pennell, Circ, 2005)
**CMR for Myocardial Viability**

**Strengths:**
- Specific signal for scar
- Highly effective in determining the etiology of HF
- High resolution defines transmural extent
- Gold standard for regional and global function
- Provides comprehensive assessment
- Easily adapted for contractile reserve
- Easily extended to perfusion/perfusion reserve

**Limitations:**
- Relatively high cost of equipment
- Technical expertise not widespread

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**Cardiac Imaging for Functional Recovery**

Myocardial Viability and Improved Survival

![Bar chart showing mortality rates for viable and non-viable myocardial regions with revascularization and medical therapy.](image)

- **24 studies**
  - n=3088
  - EF=32.9%

![Bar chart showing mortality rates for viable and non-viable myocardial regions with revascularization and medical therapy.](image)

- **28 studies**
  - n=3531
  - EF=31.5%


Surgical Treatment of Ischemic Heart Failure

Coronary-Artery Bypass Surgery in Patients with Left Ventricular Dysfunction


STICH Primary Outcome
CABG vs Medical Therapy

STICH Viability Substudy

Limitations

• STICH:
  • Designed to test for viability
  • Mandatory viability and ischemia testing
  • Due to enrollment needs
    • Viability: 601
    • Ischemia: 399

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.,
Nasiri Alotti, M.D., Ph.D., Federico M. Asch, M.D., Lilliana E. Favalaro, 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*
STICH Viability Substudy

Viability: Lower Mortality + CV Hospitalization

Univariate Multivariable

Chi-square p value Chi-square p value
20.27 <0.001 8.60 0.003

601/1202 patients; Bonow et al. N Engl J Med 2011
Viability Not Predictive of CABG Mortality Benefit

STICH Viability Substudy

Viability Not Predictive of CABG Mortality Benefit


STICH Viability Hypothesis

**SPECT protocols:**
- Thallium-201 stress-redistribution-reinjection
- Thallium-201 rest-redistribution
- Nitrate-enhanced Tc-99m perfusion imaging

**Dobutamine echo protocols:**
- Staged increase in dobutamine starting at 5 μg/kg/min
  - Testing within 90 days
  - ≥ 11/177 segments with ≤40% counts (± dysfunction
  - DSE: ≥ 5/16 dysfunction segs with improvement

**STICH Viability Substudy**

**Limitations**

- Partial sample: 601/1202 patients
- Mixed types of tests: SPECT (NTG SPECT-MPI and low-dose dobutamine echo)
- Arbitrary thresholds for viability
  - SPECT: 11/17 segs with uptake; NI function OK
  - DSE: 5/16 dysfunctional segments improving
- Not optimal viability imaging: no PET/MRI
- Duration of viability not assessed (<90 days)
- No analysis by ventricular size
- Improvement in function/QOL not assessed

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**Timeliness of revascularization in patients with hibernating myocardium**

- Hibernation/repetitive stuning are tenuous state—with myocardial cells having marginal blood flow for survival

Delay in revascularization has been associated with increased mortality rate in patients with severe left ventricular dysfunction and viable myocardium on FDG PET (Beanlands, et al Circulation 1998)
Adjusted Risk of Cardiac Death vs EF and Ischemia

Revascularization vs Medical Rx

Revascularization: all levels of ischemia

Medical therapy: 0-30% ischemia

Hachamovitch, et al
AHA 2002

RA 69 F SOB: no prior MI SH
STICH: Effect of Ischemia

- Smaller subset of STICH (n=399)
- Preliminary analysis:
  - No treatment interaction: in patients with ischemia, there was no apparent benefit of revascularization over medical therapy

  - Panza AHA abstract 2012
Can Noninvasive Cardiac Imaging Alter Patient Outcomes?

- Testing by itself does not affect outcomes
- For cardiac imaging tests to affect patient outcomes, there must be a tight linking between test result, physician action, and patient behavior; i.e., overall patient treatment.
FDG PET Imaging-Assisted Management of Patients with Severe LV Dysfunction*
(PARR-2 Trial)

FDG PET (n=218) Standard care (n=212)
FU 1 yr for cardiac death, MI, or recurrent hospital stay for cardiac cause
HR 0.78, p=0.15
*EF≤35%

Trial design: Revascularize only when extensive viability present; Only 75% adhered

Beanlands et al. JACC 2007;50:2002-12

*EF≤35%
FDG PET Imaging-Assisted Management of Patients with Severe LV Dysfunction (PARR-2 Trial)

FDG PET
[156 /207 (75%) with adherence to PET recommendations]
Standard care (n=212)
FU 1 yr for cardiac death, MI, or recurrent hospital stay for cardiac cause
HR=0.62, p=0.019)

Beanlands et al. JACC 2007;50:2002-12

Increasing Benefit From Revascularization Is Associated With Increasing Amounts of Hibernation (Substudy of PARR-2 Trial)

• Post hoc analysis included 182 patients with LVEF 35% or less and coronary artery disease, being considered for revascularization work-up, and randomized to the PET arm of PARR-2.
• The primary outcome was a composite of cardiac death, myocardial infarction, or cardiac repeat hospital stay at 1 year.
Increasing Benefit From Revascularization Is Associated With Increasing Amounts of Hibernation (Substudy of PARR-2 Trial)

D’Egidio et al. JACC: Cardiovascular Imaging 2009;2:1060-68
Increasing Benefit from Revascularization Is Associated with Increasing Amounts of Myocardial Hibernation (A Substudy of the PARR-2 Trial)

Effect of Revascularization or Medical Therapy

182 (of 207) pts (complete data) with LVEF <35\% randomized to PET (all centers)

FU 1 yr for cardiac death, MI, or cardiac repeat hospital stay:

D’Egidio et al.
*JACC* 2009;2:1060-8

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Imaging of Myocardial Viability in Patients with CAD and Severe Ventricular Dysfunction:

- **STICH**: results suggest that SPECT or DSE imaging for viability may not distinguish patients who have a survival benefit from revascularization
  - Multiple limitations to the study
- **PARR2**: results suggest that extensive viability by PET is predictive of benefit
EDITORIAL POINT OF VIEW

Myocardial viability testing: Still viable after stich?

Robert O. Bonow, MD, and Thomas A. Holly, MD

Imaging should be reserved for those patients in whom management decisions are difficult in view of age, comorbidities, or complex coronary anatomy, and in whom additional information may be necessary to guide therapy recommendations.