MPI & Myocardial Viability

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It is now understood that, among patients with ICM LV systolic dysfunction can result from myocardial necrosis, myocardial hibernation, or repetitive myocardial stunning.

While myocardial necrosis is irreversible, systolic dysfunction resulting from hibernation and stunning are potentially reversible states of ventricular dysfunction.
Most patients with chronic heart failure have an admixture of all three pathophysiologic entities.

Clinical studies have shown that viable myocardium can be demonstrated in a substantial number of pts with CHD and LV dysfunction, even in the absence of angina.
In pts. with significant amounts of viable myo., LV function may improve markedly, and even normalize, following successful revascularization.

An estimated **20 to 40%** of pts. with chronic ischemic LV dysfunction have the potential for significant improvement in LV function after revascularization.
The **outcome** following revascularization is dependent not only on the presence, but also **the extent, of viability**, and a critical threshold mass of viable myocardium may be necessary for functional recovery and prognostic benefit to occur from revascularization.
Multiple imaging techniques have been developed to assess viable and nonviable myocardium by evaluating: perfusion, cell membrane integrity, mitochondria, glucose metabolism, scar tissue, and contractile reserve.

PET, TI201 and 99mTc scintigraphy, have been extensively evaluated for assessment of viability and prediction of clinical outcome after coronary revascularization.
Imaging techniques for viability detection
<table>
<thead>
<tr>
<th>Imaging modality</th>
<th>Characteristics of viability</th>
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<tbody>
<tr>
<td>PET or SPECT with $^{18}$F-FDG</td>
<td>Glucose use</td>
</tr>
<tr>
<td>SPECT with $^{201}$TI</td>
<td>Perfusion and cell membrane integrity</td>
</tr>
<tr>
<td>SPECT with $^{99m}$Tc-labeled tracers</td>
<td>Perfusion, cell membrane integrity, and mitochondrial intactness</td>
</tr>
<tr>
<td>Contrast echocardiography</td>
<td>Perfusion</td>
</tr>
<tr>
<td>Echocardiography or MRI with low-dose dobutamine infusion</td>
<td>Contractile reserve</td>
</tr>
<tr>
<td>Contrast-enhanced MRI</td>
<td>Scar tissue</td>
</tr>
<tr>
<td>Contrast-enhanced CT</td>
<td>Scar tissue</td>
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</table>
FIGURE 2. PET with $^{13}$N-ammonia and $^{18}$F-FDG to assess myocardial viability (26). Regional myocardial $^{18}$F-FDG uptake is disproportionately enhanced compared with regional myocardial blood flow; this pattern is termed perfusion–metabolism mismatch and is indicative of hibernating myocardium.

FIGURE 3. Corresponding series of $^{201}$TI rest–redistribution SPECT short-axis slices. Early slices (top) show defect in inferoseptal wall, with redistribution on late slices (bottom).
In general, nuclear imaging techniques have a high sensitivity for the detection of viability, whereas techniques evaluating contractile reserve have a somewhat lower sensitivity and a higher specificity.
The Endpoints used in viability studies after revascularization include improvement in:

- Regional LV function (segments)
- Global LV function (LVEF)
- Symptoms (NYHA) functional class
- Exercise capacity (METS)
- Reverse LV remodeling (LV volumes)
Endpoints in Viability Studies

Improvement in LV function and survival after revascularization is still considered the final proof of viability.
In an analysis of pooled data, including 105 studies (with 3,003 pts) that focused on viability assessment (with nuclear imaging and DSE, 84% of the improved segments were considered to be viable according to the imaging modalities.)
FIGURE 1. Analysis (25) of pooled data from 24 prognostic studies that used different viability techniques and that showed 3.2% annual death rate in patients who had viable myocardium and who were undergoing revascularization, compared with 16% annual death rate in patients who had viable myocardium and who were treated medically. Intermediate event rates (7.7% and 6.2%) were observed in patients with nonviable myocardium.
Assessment of Myocardial Viability in Patients with Heart Failure

Arend F.L. Schinkel, Don Poldermans, Abdou Elhendy, and Jeroen J. Bax
The Netherlands;

Pooled Data from Viability Studies of Bax et al. with Different Techniques to Predict Improvement in LVEF After Revascularization

<table>
<thead>
<tr>
<th>Technique</th>
<th>No. of studies</th>
<th>% Sensitivity</th>
<th>% Specificity</th>
<th>% NPV</th>
<th>% PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F-FDG PET</td>
<td>20</td>
<td>93</td>
<td>58</td>
<td>85</td>
<td>77</td>
</tr>
<tr>
<td>$^{201}$TI imaging</td>
<td>33</td>
<td>87</td>
<td>55</td>
<td>81</td>
<td>64</td>
</tr>
<tr>
<td>$^{99m}$Tc-labeled tracers</td>
<td>20</td>
<td>81</td>
<td>66</td>
<td>77</td>
<td>71</td>
</tr>
<tr>
<td>DSE</td>
<td>32</td>
<td>81</td>
<td>80</td>
<td>85</td>
<td>77</td>
</tr>
</tbody>
</table>
### Pooled Data from Viability Studies of Maddahi et al. with Different Techniques to Predict Improvement in LVEF After Revascularization

<table>
<thead>
<tr>
<th>Technique</th>
<th>No. of studies (no. of patients)</th>
<th>% LVEF pre</th>
<th>% LVEF post</th>
<th>% LVEF pre</th>
<th>% LVEF post</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F-FDG PET</td>
<td>12 (333)</td>
<td>37</td>
<td>47</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>$^{201}$Tl</td>
<td>5 (96)</td>
<td>30</td>
<td>38</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>$^{99m}$Tc-labeled tracers</td>
<td>4 (75)</td>
<td>47</td>
<td>53</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>DSE</td>
<td>8 (254)</td>
<td>35</td>
<td>43</td>
<td>35</td>
<td>36</td>
</tr>
</tbody>
</table>

DSE = dobutamine stress echocardiography; post = after revascularization; pre = before revascularization.
Additional Information Needed Besides Myocardial Viability

Effect of delayed vs. timely revascularization on change in LVEF in pts with substantial viability on DSE..

Pts with early revascularization showed significant improvement in LVEF after revascularization, which was not observed after delayed revascularization.
Myocardial Viability; Dead or Alive
The Heart Failure Revascularisation Trial (HEART),

*European journal of HF 2011;13.227-233, Cleland et al*

**STICH (Surgical Treatment for Ischemic Heart Failure)**

*RO Bonow et al*

The Heart Failure Revascularisation Trial (HEART)

Only 138 of the planned 800 patients were enrolled because of withdrawal of funding due to slow recruitment. Also, a larger trial (The Surgical Treatment for Ischemic Heart Failure Trial) addressing a similar question became available, which investigators were encouraged to join.

**Conclusion** A conservative management strategy may not be inferior to one of coronary arteriography with the intent to revascularize in patients with heart failure, LV systolic dysfunction, and extensive myocardial viability. However, this study was underpowered and, further, larger trials are required to settle this issue.
Population and treatment: •

1212 pts with CAD amenable to CABG with LVEF <35%
Randomized to CABG or standard medical therapy alone

Primary outcome: •

All-cause death
STICH (Surgical Treatment for Ischemic Heart Failure)

Study Procedures

In the initial design of the STICH trial, viability testing with SPECT was required for the enrollment of patients. However, this requirement proved to be an obstacle to enrollment.

Therefore, the protocol was subsequently revised to make viability testing optional and to allow the use of either SPECT or DSE for viability testing.

Investigators at all study centers were strongly encouraged to perform viability testing in every patient, but the decision to perform the test was left up to the recruiting investigators.
Pt Follow-Up and Outcomes

After trial enrollment, pts were followed every 4 months for the first year and every 6 months thereafter. 

The primary outcome was death from any cause. 

Secondary end points included death from cardiovascular causes and a composite of death from any cause or hospitalization for cardiovascular causes.
STICH (Surgical Treatment for Ischemic Heart Failure)

For SPECT, pts with viability were defined those with 11 or more viable segments on the basis of relative tracer activity.

For DSE, pts with viability were defined as those with 5 or more segments with abnormal resting systolic function but manifesting contractile reserve during dobutamine administration.
On Univariate Analysis, there was a significant association between myocardial viability and outcome. However, this association was not significant on multivariable analysis that included other prognostic variables.

The findings of this multivariable analysis do not necessarily indicate that myocardial viability does not have pathophysiological importance in pts with CAD and LV dysfunction. Instead, it is likely that some of the other variables in the analysis (e.g., LV volumes and EF) are causally determined by the extent of viable myocardium.
**STICH (Surgical Treatment for Ischemic Heart Failure)**

**Figure 1.** Kaplan–Meier Analysis of the Probability of Death, According to Myocardial Viability Status.

The comparison that is shown has not been adjusted for other prognostic baseline variables. After adjustment for such variables on multivariable analysis, the between-group difference was not significant ($P=0.21$).
STICH (Surgical Treatment for Ischemic Heart Failure)

**Figure 2. Kaplan–Meier Analysis of the Probability of Death According to Myocardial-Viability Status and Treatment.**

At 5 years in the intention-to-treat analysis, the rates of death for patients without myocardial viability were 41.5% in the group assigned to undergo coronary-artery bypass grafting (CABG) and 55.8% in the group assigned to receive medical therapy (Panel A). Among patients with myocardial viability, the respective rates were 31.2% and 35.4% (Panel B). There was no significant interaction between viability status and treatment assignment with respect to mortality (P=0.53) (Panel C).
STICH (Surgical Treatment for Ischemic Heart Failure)

Conclusions
The presence of viable myocardium was associated with a greater likelihood of survival in patients with CAD and LV dysfunction, but this relationship was not significant after adjustment for other baseline variables.

The assessment of myocardial viability did not identify patients with a differential survival benefit from CABG, as compared with medical therapy alone.
"This is an incredible trial. A stunning achievement."
- Dr Bernard Gersh

"With the results of the STICH trial, we should be comfortable with the notion that, in general, surgery is not superior to optimal medical therapy for ischemic left ventricular dysfunction."
- Dr James Fang

*All comments from Docs say STICH "hypothesis one" supports CABG in HF patients despite missing primary end point (http://www.theheart.org/article/1205919.do) and STICH substudy: Viability testing didn't affect treatment outcomes (http://www.theheart.org/article/1204899.do)*
Conclusions that can be drawn from our results are limited by a number of factors. First, viability data were not available for all the pts who were enrolled in the STICH hypothesis 1 comparison. The study pts represent slightly less than 50% of the randomized group. Second, only 114 of 601 pts who underwent assessment of myocardial viability (19%) were deemed not to have viable myocardium on the basis of our prespecified criteria. This small number limited the power of our analysis to detect a differential effect of CABG, as compared with medical therapy, in pts with myocardial viability, as compared with those without myocardial viability.
Third, we cannot exclude the possibility that results of viability testing could have influenced subsequent clinical decision making. There was a nonsignificant trend toward higher rates of surgery among pts who underwent viability testing on the day of randomization or on the subsequent day than among those who underwent such testing before randomization.

Fourth, our analysis was based on SPECT and DSE assessment of myocardial viability.
Take Home Message

Imaging techniques in nuclear cardiology play an important role for the noninvasive evaluation of myocardial viability in pts with CAD.

In pts. with significant amounts of viable myo., LV function may improve markedly, and even normalize, following successful revascularization.
Thank You

Prof. Dr. Ahmed Abdelaty