Revascularization in Severe LV Dysfunction: The Role of Inducible Ischemia and Viability Testing

Evidence and Uncertainties

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Northwestern Memorial Hospital
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No Relationships to Disclose
CAD and Heart Failure

**Indications for revascularization:**

- Medically intractable angina
- Left main disease
- 3-vessel disease
- 2-vessel disease with proximal LAD stenosis

ESC 2010 Guidelines on Myocardial Revascularization
ACC/AHA 2011 Guidelines for Coronary Artery Bypass Graft Surgery
ACC/AHA 2013 Guideline for Management of Heart Failure
Prognosis in Chronic CAD

Influence of LV Ejection Fraction

from Muhlbaier et al, Circulation 1992;86:II-198
Prognosis in Ischemic LV Dysfunction

Increase in Survival by Revascularization

Increase in Survival (%)
Prognosis in Ischemic LV Dysfunction

Increase in Survival by Revascularization

Increase in Survival (%)
Prognosis in Ischemic LV Dysfunction

Increase in Survival by Medical Therapy

from Yancy CW, J Am Heart Assoc 2012;1:16-26
Surgical Treatment for Ischemic Heart Failure
STICH Trial

- 1212 patients with EF <35%
- 99 sites in 22 countries

**Primary Endpoint:**
All-cause mortality

**Secondary Endpoints:**
CV mortality
Death + CV hospitalization
Death + HF hospitalization
STICH Primary Outcome
All-Cause Mortality

<table>
<thead>
<tr>
<th>Medical therapy</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>0.86</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.72,1.04</td>
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<tr>
<td>P</td>
<td>0.123</td>
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STICH Secondary Outcome
Cardiovascular Mortality

STICH Secondary Outcome
Death + CV Hospitalization

<table>
<thead>
<tr>
<th></th>
<th>Medical therapy</th>
<th>CABG</th>
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<tbody>
<tr>
<td>HR</td>
<td>0.74</td>
<td>0.64</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.64, 0.85</td>
<td>0.85</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td></td>
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</tbody>
</table>

Randomized medicine

602

Randomized CABG

610

Received medicine

537

55

Early crossover

592

Randomized medicine

Received medicine

Randomized CABG

Early crossover

STICH Secondary Outcome
All Cause Mortality – Treatment Received

Doenst et al. Circ Heart Fail 2013;6:443-450
STICH Secondary Outcome
All Cause Mortality – Per Protocol

Doenst et al. *Circ Heart Fail* 2013;6:443-450

<table>
<thead>
<tr>
<th>Medical therapy</th>
<th>CABG</th>
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<tbody>
<tr>
<td>HR</td>
<td>0.76</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.62,0.92</td>
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<tr>
<td>P</td>
<td>0.005</td>
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</table>
STICH Quality of Life

KCCQ: Overall Summary

Myocardial Revascularization in Patients with LV Dysfunction

*The STICH Trial:*
Is STICH a positive trial or a negative trial?
Myocardial Revascularization in Patients with LV Dysfunction

**The STICH Trial:**
Are there subsets who benefit from CABG?
Myocardial Revascularization in Patients with LV Dysfunction

The STICH Trial: Are there subsets who benefit from CABG?

Myocardial viability
Myocardial Viability and Improved Survival

[Diagram showing mortality rates (%/year) for viable and non-viable cases with revascularization and medical treatments.]

- Viable:
  - Revascularization: 3.2 (n=748)
  - Medical: 16.0 (n=557)

- Non-Viable:
  - Revascularization: 7.7 (n=330)
  - Medical: 6.2 (n=734)

24 studies, n=3088, EF=32.9%

Myocardial Viability and Improved Survival

Mortality Rate (%/year)

Revascularization
Medical

p<0.001

Viable
Non-Viable

3.2
16.0
7.7
6.2

n=748
n=557
n=330
n=734

24 studies
n=3088
EF=32.9%

Allman et al, J Am Coll Cardiol 2002;39:1151-1158
Myocardial Viability and Improved Survival

- Viable: 3.2% (n=748) vs 7.7% (n=330), p=NS
- Non-Viable: 16.0% (n=557) vs 6.2% (n=734)

24 studies n=3088 EF=32.9%

Allman et al, J Am Coll Cardiol 2002;39:1151-1158
Myocardial Viability and Improved Survival

Myocardial Viability and Improved Survival

from Camici et al, *Circulation* 2008;117:103-114

13 studies
n=2433
EF=29.9%
Limitations of Cohort Studies

- Retrospective
- Heterogeneous methodology
- Decision for CABG may have been influenced by viability status
- No (or inadequate) adjustment for key baseline variables (age, comorbidities)
- Cohort studies carried out before modern aggressive medical therapy
Limitations of Cohort Studies

- Retrospective
- Heterogeneous methodology
- Decision for CABG may have been influenced by viability status
- No (or inadequate) adjustment for key baseline variables (age, comorbidities)
- Cohort studies carried out before modern aggressive medical therapy
LV Ejection Fraction (percent)

- Allman: 32.9% (n=3088)
- Schinkel: 31.5% (n=3531)
- Camici: 29.9% (n=2433)
- STICH: 26.7% (n=601)

References:
- Camici et al, *Circulation* 2008;117:103-114
Medical Therapy in Patients with Viable Myocardium

Allman et al, J Am Coll Cardiol 2002;39:1151-1158
Camici et al. Circulation 2008;117:103-114
Myocardial Viability and Mortality

Myocardial Viability and Mortality

Myocardial Viability and Mortality

Mortality + CV Hospitalization

Viability testing does identify high risk patient subgroups and predicts:

- Response to beta blocker therapy
- Response to revascularization

Viability testing should not be considered a prerequisite for decisions regarding medical versus surgical management in patients with ischemic LV dysfunction
Heart Failure

Myocardial Viability Testing and the Effect of Early Intervention in Patients With Advanced Left Ventricular Systolic Dysfunction

Khalidoun G. Tarakji, M. Obadah Al-Chekaki, Eugene

Revascularization vs Medical Therapy in Patients with Left Ventricular Dysfunction

n=306

from Tarakji et al, Circulation 2006;113:230-237
The Heart Failure Revascularisation Trial (HEART)

John G.F. Cleland, Melanie C. Bjarnason, Stephen G. Ball, Robert S. Bragg, Dudley J. Pennell, and Robert D. Bristow

European Journal of Heart Failure (2011) 13, 227–233
doi:10.1093/eurjhf/hfq230

Revascularization vs Medical Therapy in Patients with Myocardial Viability

n=138
p=NS

Survival (percent)

Revascularization (n=69)
Medical therapy (n=69)

Time (years)

from Cleland et al, Eur J Heart Fail 2011;13:227-233
Myocardial Revascularization in Patients with LV Dysfunction

The STICH Trial: Are there subsets who benefit from CABG?

Myocardial ischemia
Myocardial Ischemia and Mortality

Subgroup | N | Deaths | HR | 95% CI | Interaction P value
--- | --- | --- | --- | --- | ---
Without ischemia | 143 | 58 | 0.72 | 0.42, 1.25 | 0.643
With ischemia | 256 | 103 | 0.83 | 0.56, 1.23 | 0.25

Panza et al. *J Am Coll Cardiol* 2013;61:1860-1870
Impact of Ischemia and Scar on Therapeutic Benefit of Coronary Revascularization

Hachamovich et al, *Eur Heart J* 2011;32:1012-1024
Impact of Ischemia and Scar on Therapeutic Benefit of Coronary Revascularization

- Magnitude of ischemic myocardium associated with survival benefit with revascularization in patients without prior MI
- No such benefit in patients with prior MI
- Role of ischemia not significant in patients with >10% myocardial scar

Hachamovich et al, Eur Heart J 2011;32:1012-1024
Myocardial Revascularization in Patients with LV Dysfunction

*The STICH Trial:* Are there subsets who benefit from CABG?

Biomarkers?
Brain Natriuretic Peptide Levels

Feldman et al, *Circ Heart Fail* 2013;6:461-472
Tumor Necrosis Factor-α Receptor-1

Feldman et al, *Circ Heart Fail* 2013;6:461-472
Myocardial Revascularization in Patients with LV Dysfunction

The STICH Trial: Are there subsets who benefit from CABG?

Functional capacity?
6-Minute Walk and Physical Activity Score

<table>
<thead>
<tr>
<th>PAS &gt;55 + 6MW ≥300m</th>
<th>PAS ≤55 + 6MW &lt;300m</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MED</strong></td>
<td><strong>MED</strong></td>
</tr>
<tr>
<td><strong>CABG</strong></td>
<td><strong>CABG</strong></td>
</tr>
<tr>
<td><strong>Hazard ratio</strong> 0.71</td>
<td><strong>Hazard ratio</strong> 0.95</td>
</tr>
<tr>
<td>95% CI 0.52,0.97</td>
<td>95% CI 0.75,1.19</td>
</tr>
<tr>
<td><strong>P-value</strong> 0.033</td>
<td><strong>P-value</strong> 0.626</td>
</tr>
</tbody>
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Interaction P value = 0.167

Stewart et al. *JACC Heart Fail* 2014;2:335-343
Myocardial Revascularization in Patients with LV Dysfunction

The STICH Trial:
Are there subsets who benefit from CABG?

Severity of CAD and LV remodeling?
Extent of CAD, EF, ESV and Mortality

Comparison between MED and CABG:
- **2 – 3 Factors**
  - MED (31 deaths)
  - Hazard ratio: 0.71, 95% CI: 0.36-0.89, P-value: 0.0004
  - CABG (22 deaths)
  - Hazard ratio: 0.39

- **0 – 1 Factor**
  - MED (56 deaths)
  - Hazard ratio: 1.08, 95% CI: 0.81-1.44, P-value: 0.591
  - CABG (47 deaths)
  - Hazard ratio: 0.30

Interaction P value = 0.022

Panza et al. *J Am Coll Cardiol* 2014;64:553-561
Myocardial Revascularization in Patients with LV Dysfunction

Factors to consider:

More important:
- Severity of LV dysfunction
- Severity of LV remodeling
- Angiographic severity of CAD
- Functional capacity

Less important:
- Extent of myocardial viability
- Severity of myocardial ischemia
- Biomarkers
2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease


Patients with LV dysfunction

CABG  
IIa—EF 35% to 50%  B

CABG  
IIb—EF <35% without significant left main CAD  B

PCI  
Insufficient data
Patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction \( \leq 35\% \)) presenting predominantly with heart failure symptoms

<table>
<thead>
<tr>
<th>Class(^a)</th>
<th>Level(^b)</th>
<th>Ref.(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG should be considered in the presence of viable myocardium, irrespective of LVESV.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>PCI may be considered if anatomy is suitable, in the presence of viable myocardium.</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Revascularization in the absence of evidence of myocardial viability is not recommended.</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>
2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Chest Physicians, Heart Rhythm Society and International Society for Heart and Lung Transplantation

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation

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Mild to moderate LV systolic dysfunction (EF 35% to 50%)<br>

**class IIa**<br>

CABG to improve survival is reasonable in patients with significant multivessel CAD or proximal LAD coronary artery stenosis when viable myocardium is present in the region of intended revascularization. (*LOE: B*)
Mild to moderate LV systolic dysfunction (EF 35% to 50%)

**class IIa**

CABG to improve survival is reasonable in patients with significant multivessel CAD or proximal LAD coronary artery stenosis when viable myocardium is present in the region of intended revascularization. *(LOE: B)*

Severe LV systolic dysfunction (EF <35%)

**class IIa**

CABG or medical therapy is reasonable to improve morbidity and CV mortality in patients with significant CAD. *(LOE: B)*
Surgical/Percutaneous/Transcatheter Interventional Treatments of HF: Recommendations

Mild to moderate LV systolic dysfunction (EF 35% to 50%)

**class IIa**

CABG to improve survival is reasonable in patients with significant multivessel CAD or proximal LAD coronary artery stenosis when viable myocardium is present in the region of intended revascularization. *(LOE: B)*

Severe LV systolic dysfunction (EF <35%)

**class IIa**

CABG or medical therapy is reasonable to improve morbidity and CV mortality in patients with significant CAD. *(LOE: B)*

**class IIb**

CABG may be considered with the intent of improving survival in patients with CAD and operable coronary anatomy whether or not viable myocardium is present. *(LOE: B)*
**Treatment of Stages A to D**

**Stage A: Recommendations**

1. Hypertension and lipid disorders should be controlled in accordance with contemporary guidelines to lower the risk of HF. *(LOE: A)*

2. Other conditions that can lead or contribute to HF, such as obesity, diabetes mellitus, tobacco use, and known cardiotoxic agents, should be controlled or avoided. *(LOE: A)*

**Stage B: Recommendations**

1. In all patients with recent of remote history of MI or ACS and reduced EF, ACE inhibitors, evidence-based beta blockers, and statins should be used to prevent symptomatic HF and reduce mortality. *(LOE: A)*