CABG & OMT Evolving Again?

Microcirculation & OMT+Adherence

New York, Dec 9, 2016

No Disclosures
Revascularization for CAD

OMT vs CABG+OMT vs PCI+OMT

1980’s.
- LMD, The Rule of 2 / 3 – CABG
  - Moderate <LVEF
  - Severe Ischemia
  - 3 Vessel Disease or 2vd + pLAD
  - Severe - Yes, STICH
  - Moderate – COURAGE OMT ISCHEMIA
  - 12vd in DM

1990’s.
- The Rule of 2 / 3 – PCI?

2000’s.
- PCI <, CABG > (DM), Microc., OMT

2020’s.
- Anatomical, Isch.Score, Microc.: Ninv. - OMT+
Revascularization for CAD
OMT vs CABG+OMT vs PCI+OMT

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2020,s. Anatomical, Isch.Score, Microc.: Ninv. - OMT+
# COMPLEX, STABLE CORONARY DISEASE

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>MVD</th>
<th>DM</th>
<th>INTERV.</th>
<th>MT.</th>
<th>EP.-R</th>
<th>Data</th>
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<tbody>
<tr>
<td>SYNTAX</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>CABG &gt; PCI</td>
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<td></td>
<td>SYNTAX Score</td>
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<tr>
<td>FAME</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>PCI</td>
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<td></td>
<td></td>
<td></td>
<td>&quot;ISCHEMIA&quot; Score</td>
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<tr>
<td>BARI</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>CABG / PCI = MT</td>
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<tr>
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<td></td>
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<td>X.OV.ER 42%</td>
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<tr>
<td>COURAGE</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>PCI = MT – X-OVER</td>
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<td></td>
<td>&quot;ISCHEMIA&quot; &gt;10% -Events</td>
</tr>
<tr>
<td>FREEDOM</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>(+)</td>
<td>+</td>
<td>CABG &gt; PCI</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>No Freedom of Choice?</td>
</tr>
</tbody>
</table>

**Conditions** | **Methods-Interests** | **Conclusions**
Baseline SYNTAX Score Tercile - CABG Cumulative Event Curves For MACCE

SYNTAX (FW Mohr, PW Serruys et. al.) Lancet 2013; 381: 629
**FFR As A Surrogate For Inducible Myocardial Ischaemia**

**FAME I** (FFR > 0.8) - OMT of Non-Isch. Les. – Prevent MI/Death

**FAME II** (FFR < 0.8) - PCI Isch. Les. – Prevent MI/Death

FAME: CUMULATIVE EVENTS DURING 5-YEAR FOLLOW-UP

FAME (LX van Nunen et al., The Lancet 2015; 386:1853)
Distribution of Coronary Stenosis Severity Relation To Fractional Flow Reserve

S Gaur et. al. Eur Heart J. 2016;37:1220
Coronary Flow Reserve (CFR)

- Measures integrated hemodynamic effects of epicardial CAD, diffuse atherosclerosis, vessel remodeling and microvascular dysfunction on myocardial tissue perfusion.

\[
CFR = \frac{MBF_{\text{peak hyperemia}}}{MBF_{\text{rest}}}
\]

VR Taqueti and MF Di Carli 2014
Coronary Vascular Regulation, Remodelling, And Collateralization

AR Pries et al. Eur Heart J. 2015;36:3134
Working Group On Coronary Pathophysiology And Microcirculation
The microcirculation is responsible for orchestrating adjustments in vascular tone to match local tissue perfusion with oxygen demand. The concept is put forth that vasculoparenchymal communication is multinodal, with vascular release of nitric oxide eliciting dilation and preserving normal parenchymal function by inhibiting inflammation and proliferation. Likewise, in disease or stress, endothelial release of reactive oxygen species mediates both dilation and parenchymal inflammation leading to cellular dysfunction, thrombosis, and fibrosis. This paradigm may help explain why microvascular dysfunction is such a powerful predictor of cardiovascular events and help identify new approaches to treatment and prevention.

DD Gutterman et al., Circ Res 2016; 118:157
A1. 17-segment Coronary Flow Reserve PET (Epic. vs Microv.?)
Multiparametric Cardiovascular Magnetic Resonance Assessment of Cardiac Allograft Vasculopathy

Christopher A. Miller, BSc, MBChB,† ‡ Jaydeep Sarma, MA, MB BCHIR, PhD,‡§ Josephine H. Naish, PhD,† Nizar Yonan, MD,‡ ‡ Simon G. Williams, MD,‡ ‡ Steven M. Shaw, PhD,‡ ‡
David Clark, BSc,§ Keith Pearce, BSc,‡ Martin Stout, PhD,† Rahul Potluri, MBChB,‡ ‡
Alex Borg, MD,‡ Glyn Coutts, PhD,¶ Saqib Chowdhary, PhD,‡ ‡ Gerry P. McCann, MD,¶
Geoffrey J. M. Parker, PhD,† Simon G. Ray, MD,‡ ‡ Matthias Schmitt, MD, PhD‡ ‡
Manchester and Leicester, United Kingdom

Diagnostic Accuracy of Myocardial Magnetic Resonance Perfusion to Diagnose Ischemic Stenosis With Fractional Flow Reserve as Reference Systematic Review and Meta-Analysis

Min Li, MD, Tao Zhou, MD, Lin-feng Yang, MD, Zhao-hui Peng, MD, Juan Ding, MD, Gang Sun, MD, PhD
A3. Diagnostic Evaluation of Chest Pain
Clinical Implications From SCOT-HEART and PROMISE

SCOT-HEART and PROMISE represent the 2 largest and most comprehensive CV imaging outcome trials in patients with stable chest pain and provide significant insights into patient diagnosis, management, and outcomes. The overall goal was to better inform the practicing clinician in the selection of noninvasive testing for stable chest pain. Similarities and differences between SCOT-HEART and PROMISE are highlighted, and clinical and practical implications are discussed. Both trials show that CT angiography should have a greater role in the diagnostic pathway of patients with stable chest pain.

CB Fordyce et al., JACC 2016; 67:843
In symptomatic patients with suspected CAD, CTA improves patient selection for invasive CA compared with functional testing. The impact of measuring by CTA (FFR<sub>CT</sub>) is unknown. At 11 sites, 584 patients with new onset chest pain were prospectively assigned to receive either usual testing (n=287) or CTA/FFR<sub>CT</sub>(n=297). Test interpretation and care decisions were made by the clinical care team. CTA/FFR was a feasible and safe alternative to ICA and was associated with a significantly lower rate of invasive angiography showing no obstructive CAD.

**PLATFORM** (PS Douglas et al.) Eur Heart J 2015; 36:3359
In symptomatic patients with suspected CAD, CTA improves coronary calcification was assessed by using the Agatston score (AS) in 214 patients suspected of having CAD who underwent coronary CTA, FFR_{CT}, and FFR. The diagnostic performance of FFR_{CT} (≤0.80) in identifying vessel-specific ischemia (FFR ≤0.80) was investigated across AS quartiles. FFR_{CT} provided high and superior diagnostic performance compared with coronary CTA interpretation alone.

*NXT Trial* (BL Nørgaard et al.), *J Am Coll Cardiol Img* 2015; 8:1045
B1. Impaired CFR & Zero CAC - MACE

Non-obstructive CAD

MACE 57/901, follow up 1.5 years

P=0.24, CAC
P=0.002, CFR

Adjusted MACE (%/yr)

- CAC 0
  - CFR ≥2.0: 1.4%
  - CFR <2.0: 5.2%
  - N=214

- CAC 1-399
  - CFR ≥2.0: 1.8%
  - CFR <2.0: 4.8%
  - N=163

- CAC ≥400
  - CFR ≥2.0: 3.6%
  - CFR <2.0: 7.5%
  - N=53

B2. Diabetes - CFR w/wo Epicardial CAD, Relation To Cardiac Death

![Graph showing annualized cardiac mortality with and without diabetes and coronary flow reserve (CFR) in CAD patients.]

- CAD+/DM+ (N=606): 2.9% annualized cardiac mortality, P=0.07
- CAD+/DM- (N=569): 2.0% annualized cardiac mortality, P=0.33
- CAD-/DM+ CFR ≤1.6 (N=227): 2.8% annualized cardiac mortality, P=0.005
- CAD-/DM+ CFR >1.6 (N=339): 0.3% annualized cardiac mortality, P=0.65
- CAD-/DM- NI MPI/EF (N=682): 0.5% annualized cardiac mortality

B3. Prognostic Value of Microvascular Obstruction and Infarct Size, as by CMR in STEMI Patients

MO - Visualized With Late Gadolinium Enhancement, Defined As Any Region Of Hypoenhancement Within The Hyperenhanced Area

M van Kranenberg et al. J Am Coll Cardiol Img 2014;7:930
B4. Angina During Follow-up

**FREEDOM** (MS Abdallah, V Fuster et. al.) JAMA. 2013;310(15):1581

**SJ Head et. al. EHJ. 2014;35:2821 – Usually, Angina in PCI > CABG**
B5. Proportion of Outcome Event by Achieved SBP - ONTARGET Trial

ONTARGET (J Redon et al.) JACC 2012; 59:74 – Microvasculature, Underperfusion?

FREEDOM (M Farkouh, V Fuster) 2016 (In Press)
B6. Mortality in the ACCORD Population Over a Range of On-treatment HbA1c Values

Adjusted log(Hazard Ratio) by Treatment Strategy Relative to Standard at A1c of 6%

ACCORD (MC Riddle et al) Circ 2010;122:844 - Microvascular / Catecholamines
B7. PCI versus CABG in Insulin and Non-Insulin Treated Diabetic Patients: Results from FREEDOM

FREEDOM (GD Dangas, V Fuster et al.) JACC 2014; 64: 1189
EM Jeong et. al. Circ J 2015; 79: 470
Fifty-seven diabetic patients with CAD, classified as non-DR (n=42) or DR (n=15), underwent angioscopic observation of at least 1 entire coronary artery. The number of yellow plaques (NYP) through the observed coronary artery was counted and their color grades, defined as 1 (light yellow), 2 (yellow), or 3 (intense yellow), were evaluated. The association between the presence of DR and incidences of acute coronary syndrome (ACS) was analyzed during the follow-up period (mean 7.1 ± 3.3 years). Our findings indicate that coronary atherosclerosis and plaque vulnerability are more severe in patients with DR. DR as a microvascular complication may be directly linked with macrovascular plaque vulnerability & fatal events such as ACS.

O Kurihara et al., Am J Cardiol 2016; 118:944
Comparisons Of Coronary Atherosclerosis On Angioscopy

O Kurihara et. al. Am J Cardiol 2016;118:944
Impact of Diabetic Retinopathy on Vulnerability of Atherosclerotic Coronary Plaque & Incidence of ACS

O Kurihara et. al. Am J Cardiol 2016;118:944
Routes Of Gene Therapy To The Retina

**B10. Chest Pain Without Obstructive CAD**

MA Marinescu et. al. J Am Coll Cardiol Img 2015;8:210
### Conditions Linked to Microvascular Dysfunction

<table>
<thead>
<tr>
<th>Ischemic cardiomyopathy</th>
<th>Stress-related cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Systemic lupus erythematosis</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>Cerebral vasospasm</td>
</tr>
<tr>
<td>HfPEF</td>
<td>Tumor angiogenesis</td>
</tr>
<tr>
<td>HFReF</td>
<td>No-reflow phenomenon</td>
</tr>
<tr>
<td>Aging</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Tobacco abuse</td>
</tr>
<tr>
<td>Dementia</td>
<td>Hypertrophic obstructive cardiomyopathy</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>Obesity</td>
</tr>
<tr>
<td>Chagas disease</td>
<td>Systemic sclerosis</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Chronic thromboembolic pulmonary</td>
<td>Idiopathic cardiomyopathy</td>
</tr>
</tbody>
</table>
B11. The Prognostic Role of Coronary Microvascular Obstruction

**B12. Potential Benefit of Revascularization for Low CFR**

The figure compares the adjusted annual event rates across different groups based on coronary flow reserve (CFR) and revascularization status.

- **CFR High/No Revasc (n=79):** 6.04%, p=0.32
- **CFR High/PCI (n=70):** 3.83%, p=0.22
- **CFR High/CABG (n=17):** 2.16%, p=0.48
- **CFR Low/No Revasc (n=57):** 11.52%, p=0.17
- **CFR Low/PCI (n=84):** 7.38%, p=0.006
- **CFR Low/CABG (n=22):** 0.88%

The p-values indicate significance in the difference of event rates between the groups. For example, the difference between CFR High/No Revasc and CFR Low/No Revasc is significant (p=0.001).

NP Johnson et al. JACC. 2016;67:2772
## B13. Angiographic Classification of CAD

<table>
<thead>
<tr>
<th>CHD Stages</th>
<th>Description</th>
<th>Risk of MI or CV Death/Year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage 0</strong></td>
<td>No coronary atherosclerotic disease by coronary angiography</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td><strong>Stage 1</strong></td>
<td>Mild coronary atherosclerotic disease: &lt;30% lumen stenosis affecting 1 or 2 vessels</td>
<td>0.1-0.9</td>
</tr>
<tr>
<td></td>
<td>Moderate coronary atherosclerotic disease: 30-49% lumen stenosis affecting 1 or 2 vessels; or mild disease in 3 vessels</td>
<td>1-1.9</td>
</tr>
<tr>
<td><strong>Stage 2</strong></td>
<td>Severe coronary atherosclerotic disease: ≥50% lumen stenosis affecting 1 or 2 vessels; or moderate disease in 3 vessels</td>
<td>2-4</td>
</tr>
<tr>
<td><strong>Stage 3</strong></td>
<td>Very severe coronary atherosclerotic disease: ≥50% lumen stenosis affecting 3 vessels, or 2 vessels including pLAD, or LM disease</td>
<td>&gt;4</td>
</tr>
<tr>
<td>TRIAL</td>
<td>MVD</td>
<td>DM</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
<td>----</td>
</tr>
<tr>
<td>SYNTAX</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>FAME</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BARI</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>COURAGE</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FREEDOM</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Conditions**

**Methods-Interests**

**Conclusions**
PCI and Long-Term Survival in Patients with Stable Ischemic Heart Disease

Unadjusted hazard ratio for death, PCI plus medical therapy vs. medical therapy alone, 0.98 (95% CI, 0.83–1.15) P=0.79 by log-rank test

<table>
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<tr>
<th>Years in Study</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
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<tr>
<td>No. at Risk</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Optimal medical therapy</td>
<td>1138</td>
<td>1072</td>
<td>869</td>
<td>590</td>
<td>455</td>
<td>403</td>
<td>280</td>
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<tr>
<td>PCI plus optimal medical therapy</td>
<td>1149</td>
<td>1088</td>
<td>894</td>
<td>620</td>
<td>486</td>
<td>416</td>
<td>302</td>
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COURAGE (SP Sedlis et. al.) NEJM 2015;373:1937-53% of the original
### COMPLEX, STABLE CORONARY DISEASE

<table>
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<tr>
<th>TRIAL</th>
<th>MVD</th>
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<tbody>
<tr>
<td><strong>SYNTAX</strong></td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td><strong>CABG &gt; PCI</strong></td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SYNTAX Score</td>
</tr>
<tr>
<td><strong>FAME</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td><strong>PCI</strong></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>“ISCHEMIA” Score</td>
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<tr>
<td><strong>BARI</strong></td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td><strong>CABG / PCI = MT</strong></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
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<td>X.OV.ER 42%</td>
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<tr>
<td><strong>COURAGE</strong></td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td><strong>PCI = MT</strong></td>
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<tr>
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<td></td>
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<td>“ISCHEMIA” &gt; 10%-Events</td>
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<tr>
<td><strong>FREEDOM</strong></td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>(+)</td>
<td>+</td>
<td><strong>CABG &gt; PCI</strong></td>
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<tr>
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<td></td>
<td>No Freedom of Choice?</td>
</tr>
</tbody>
</table>

### Conditions

- **MVD**: Myocardial Vascular Disease
- **DM**: Diabetes Mellitus
- **INTERV.**: Intervention
- **MT.**: Myocardial Test
- **EP.-R**: Event Rate

### Methods-Interests

- **CABG**: Coronary Artery Bypass Graft
- **PCI**: Percutaneous Coronary Intervention

### Conclusions

- **CABG > PCI**: CABG is better than PCI
- **PCI > CABG**: PCI is better than CABG
- **CABG & PCI**: Both procedures are comparable

---

- **CABG > PCI SYNTAX Score**: CABG is preferred over PCI based on SYNTAX Score
- **PCI “ISCHEMIA” Score**: PCI is preferred over CABG based on “ISCHEMIA” Score
- **CABG / PCI = MT X.OV.ER 42%**: CABG and PCI have similar outcomes with a 42% crossover rate
- **PCI = MT “ISCHEMIA” > 10%-Events**: PCI is preferred over CABG based on “ISCHEMIA” > 10% Events
- **CABG > PCI No Freedom of Choice?**: CABG is preferred over PCI, but the choice is not free

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- **Green Circle**: Conditions
- **Yellow Circle**: Methods-Interests
- **Red Circle**: Conclusions
FREEDOM TRIAL – MI / DEATH / STROKE

Death/Stroke/MI, %

PCI/DES
CABG

Logrank P=0.005

5-Year Event Rates: 26.6% vs. 18.7%

New Engl. J. Med. 2012; 367: 2375 – All Subgroups (Syntax etc)
### 1. ACC/AHA - Recommendations for CAD Revascularization In Patients with Diabetes

<table>
<thead>
<tr>
<th>2012 Recommendation</th>
<th>2014 Focused Update Recommendations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class IIa</strong></td>
<td><strong>Class I</strong></td>
<td>New recommendation</td>
</tr>
<tr>
<td>1. CABG is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus, particularly if a LIMA graft can be anastomosed to the LAD artery. (Level of Evidence: B)</td>
<td>1. A Heart Team approach to revascularization is recommended in patients with diabetes mellitus and complex multivessel CAD. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. CABG is generally recommended in preference to PCI to improve survival in patients with diabetes mellitus and multivessel CAD for which revascularization is likely to improve survival (3-vessel CAD or complex 2-vessel CAD involving the proximal LAD), particularly if a LIMA graft can be anastomosed to the LAD artery, provided the patient is a good candidate for surgery. (Level of Evidence: B)</td>
<td>Modified recommendation (Class of Recommendation changed from IIa to I, wording modified, additional RCT added).</td>
</tr>
</tbody>
</table>
### Specific Recommendations For Revascularization In Patients With Diabetes

The Task Force on Myocardial Revascularization of the **ESC and the EACTS** (S Windecker et. al.) Eur Heart J. 2014;35:2541

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients presenting with STEMI, primary PCI is recommended over fibrinolysis if it can be performed within recommended time limits.</td>
<td>I</td>
<td>A</td>
<td>363</td>
</tr>
<tr>
<td>In patients with NSTE-ACS, an early invasive strategy is recommended over non-invasive management.</td>
<td>I</td>
<td>A</td>
<td>180,338, 364–366</td>
</tr>
<tr>
<td>In stable patients with multivessel CAD and/or evidence of ischaemia, revascularization is indicated in order to reduce cardiac adverse events.</td>
<td>I</td>
<td>B</td>
<td>93,367</td>
</tr>
<tr>
<td>In patients with stable multivessel CAD and an acceptable surgical risk, CABG is recommended over PCI.</td>
<td>I</td>
<td>A</td>
<td>106,175,349</td>
</tr>
<tr>
<td>In patients with stable multivessel CAD and SYNTAX score ≤22, PCI should be considered as alternative to CABG.</td>
<td>IIa</td>
<td>B</td>
<td>346,350</td>
</tr>
<tr>
<td>New-generation DES are recommended over BMS.</td>
<td>I</td>
<td>A</td>
<td>351,352</td>
</tr>
<tr>
<td>Bilateral mammary artery grafting should be considered.</td>
<td>IIa</td>
<td>B</td>
<td>368</td>
</tr>
<tr>
<td>In patients on metformin, renal function should be carefully monitored for 2 to 3 days after coronary angiography/PCI.</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>
The High-risk Patient Population With Indications For Revascularization Who May Be Considered For PCI

A patient-level pooled analysis was undertaken in 3 federally-funded trials. The primary endpoint was the composite of death, MI, or stroke, adjusted for trial and randomization strategy. Among 5,034 subjects, 15% had LVEF <50%, 77% had multivessel CAD, and 28% had proximal left anterior descending artery involvement. During a median 4.5-year follow-up, CABG + OMT was superior to PCI + OMT for the primary endpoint, death but not stroke. CABG + OMT reduced the primary endpoint during long-term follow-up in patients with type 2 diabetes and stable CAD, supporting this as the preferred management strategy.

GBJ Mancini, ME Farkouh, V Fuster et al., J Am Coll Cardiol 2016 68:985
CABG vs Stents For Diabetic Multivessel Disease FU 5 yrs

<table>
<thead>
<tr>
<th>Death/MI/Stroke</th>
<th>Myocardial Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG + OMT Better</td>
<td>PCI + OMT Better</td>
</tr>
<tr>
<td>p-value = 0.0002</td>
<td>p-value = 0.0001</td>
</tr>
<tr>
<td>CABG + OMT Better</td>
<td>OMT Better</td>
</tr>
<tr>
<td>p-value = 0.022</td>
<td>p-value = 0.0001</td>
</tr>
<tr>
<td>PCI + OMT Better</td>
<td>OMT Better</td>
</tr>
<tr>
<td>p-value = 0.18</td>
<td>p-value = 0.41</td>
</tr>
</tbody>
</table>

Patient-level meta-analysis to compare the effect of CABG versus PCI with DES on long-term mortality in 1,275 nondiabetic patients with multivessel CAD. Individual patient data from the SYNTAX and the BEST trials were pooled. The primary outcome was death from any cause. The median follow-up time was 61 months. The risk of death from any cause was significantly lower in the CABG group than in the PCI group. A similar finding was observed for the risk of death from cardiac causes. The superiority of CABG over PCI was consistent across the major clinical subgroups. Likewise, the rate of MI was remarkably lower after CABG than after PCI. However, the rate of stroke was not different between the 2 groups. Repeat revascularization was significantly lower in the CABG group than in the PCI group.

M Chang, S-J Park et al., J Am Coll Cardiol 2016; 68:29
CABG vs Stents For Non-diabetic Multivessel Disease

B. Death, Myocardial Infarction, or Stroke

Log-rank p = 0.011

<table>
<thead>
<tr>
<th>Patients at Risk</th>
<th>Years</th>
<th>Cumulative Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>10.0%</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>12.5%</td>
</tr>
</tbody>
</table>

CABG: 638 582 550 508 455 296
PCI: 637 592 551 505 447 285

M Chang et. al. J Am Coll Cardiol 2016;68 (In Press)
CABG vs Stents For Non-diabetic Multivessel Disease

A. Myocardial Infarction

Log-rank P<0.001

Cumulative Incidence, %

Patient at risk
CABG  PCI

M Chang et. al. J Am Coll Cardiol 2016;68 (In Press)
CABG vs Stents For Non-diabetic Multivessel Disease

A. Death

<table>
<thead>
<tr>
<th>Patients at Risk</th>
<th>Cabg</th>
<th>Pci</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>638</td>
<td>637</td>
</tr>
<tr>
<td>1</td>
<td>608</td>
<td>616</td>
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<tr>
<td>2</td>
<td>578</td>
<td>581</td>
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<tr>
<td>3</td>
<td>540</td>
<td>540</td>
</tr>
<tr>
<td>4</td>
<td>485</td>
<td>487</td>
</tr>
<tr>
<td>5</td>
<td>316</td>
<td>314</td>
</tr>
</tbody>
</table>

Log-rank p = 0.037

M Chang et. al. J Am Coll Cardiol 2016;68 (In Press)
Paclitaxel-Eluting vs Everolimus-Eluting Coronary Stents in Diabetes

C Cardiac Death or Target-Vessel Myocardial Infarction

Hazard ratio, 1.69 (95% CI, 1.04–2.75)  
P=0.03 by log-rank test  
P=0.38 for noninferiority by F–M test

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>Paclitaxel-eluting stent</th>
<th>Everolimus-eluting stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>2.5</td>
<td>4.3</td>
</tr>
<tr>
<td>6</td>
<td>3.9</td>
<td>5.1</td>
</tr>
<tr>
<td>9</td>
<td>4.2</td>
<td>5.9</td>
</tr>
<tr>
<td>12</td>
<td>4.3</td>
<td>6.7</td>
</tr>
</tbody>
</table>

No. at Risk
- Paclitaxel-eluting stent: 914, 843, 824, 798, 723
- Everolimus-eluting stent: 916, 857, 849, 825, 739

TUXEDO-India (U Kaul et. al.) NEJM 2015;373:1709
Diminishing Mortality Gap Between PCI and CABG For Multivessel Disease From the NY State Registries

- (JACC 1999) POBA
- (NEJM 2005) BMS
- (NEJM 2008) 1st Gen DES
- (NEJM 2015) 2nd Gen DES

40-50% → 24-36% → 20-29% → NS

Favors PCI
Favors CABG

### 3. ADHERENCE FOR RISK FACTOR CONTROL?

#### Risk Factors - Proportion of Participants at Goal % – 1 year

<table>
<thead>
<tr>
<th>Trials</th>
<th>LDL</th>
<th>SBP</th>
<th>DBP</th>
<th>Hb A1C</th>
<th>Meet Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base</td>
<td>FU</td>
<td>Base</td>
<td>FU</td>
<td>Base</td>
</tr>
<tr>
<td>BARI-2D</td>
<td>75</td>
<td>56</td>
<td>70</td>
<td>52</td>
<td>14</td>
</tr>
<tr>
<td>COURAGE</td>
<td>51</td>
<td>55</td>
<td>55</td>
<td>59</td>
<td>12</td>
</tr>
<tr>
<td>FREEDOM</td>
<td>55</td>
<td>63</td>
<td>53</td>
<td>55</td>
<td>12</td>
</tr>
</tbody>
</table>

Freedom, Bari-2D, Courage Investigators, JACC 2013; 61:1607

PURE (S Yusuf et al.) Lancet 2011; Aug 28 - Poor Countries, 7% !!!

NHANES, AHA, NHLBI-JNC-7, NHLBI-NCEP – Significant < Adherence

P Muntner, V Fuster et al., AHJ 2011; 161: 719 – 49 seconds !!!!
CV Drugs Underuse - Polypill, 2ary Prevention.

Argentina
Brazil
Paraguay
Italy
Spain

FOCUS 1 & 2

Food Interaction
Pharmacokinetic Interaction with Aspirin
Pharmacokinetic Interaction with Simvastatin
Pharmacokinetic Interaction with Ramipril
Pharmacodynamic Interaction with Aspirin
Pharmacodynamic Interaction with Simvastatin
Pharmacodynamic Interaction with Ramipril
Bio-equivalence

ASA, Statin, ACE-Inhibitor

Approved in 27 Countries

Am. H J 2011;162:811
JACC, 2014; 64:2071

HOPE-3-NEJM 2016;374:2032 – Polypill for 1ary Prevention?
CABG Versus PCI - Impact of Adherence to Medical Therapy on Comparative Outcomes

All non-STEMI patients undergoing revascularization in an 8-hospital network were followed for up to 8 years. Among the 973 CABG and 2255 PCI patients. There was a significant benefit for antiplatelet, lipid-lowering, and β-blocker therapy in both the CABG and PCI groups. Compliance with optimal medical therapy as a more powerful predictor of major adverse cardiac event-free survival than choice of therapy. Among comparable patients who adhere to optimal medical therapy, outcomes of PCI and CABG may not differ; however, among nonadherent patients, CABG affords better major adverse cardiac event-free survival.

P Kurlansky, M Mack et al., Circulation 2016; 134:1238
Effect of Adherence In Patients Who Underwent CABG

**A** CABG: Effect of ASA Usage Pattern on MACE Free Fraction

- **p = 0.001** (log-rank test)
- ASA - OMT
- ASA - Not OMT

Followup (mos):

<table>
<thead>
<tr>
<th>0</th>
<th>0</th>
<th>0</th>
<th>0</th>
<th>0</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>

**B** CABG: Effect of LLA Usage Pattern on MACE Free Fraction

- **p = 0.001** (log-rank test)
- LLA - OMT
- LLA - Not OMT

Followup (mos):

<table>
<thead>
<tr>
<th>0</th>
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<th>0</th>
<th>0</th>
<th>0</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>

**C** CABG: Effect of BB Usage Pattern on MACE Free Fraction

- **p = 0.001** (log-rank test)
- BB - OMT
- BB - Not OMT

Followup (mos):

<table>
<thead>
<tr>
<th>0</th>
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<th>0</th>
<th>0</th>
<th>0</th>
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<tbody>
<tr>
<td>20</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>
Effects Of DAPT, Lipid-lowering Agent (LLA) Therapy, And B-blockers In Patients Who Underwent PCI
Survival Free From MACE In Matched Patients And Optimal Antiplatelet And Lipid-lowering Regimen
4. DAPVs. Aspirin Alone After CABG In Diabetics With MVD: FREEDOM Trial Insights

S van Diepen, V Fuster, ME Farkouh et al., JACC 2016 (In Press)
Revascularization for Coronary Artery Disease

**OMT vs PCI vs CABG**

<table>
<thead>
<tr>
<th>Year</th>
<th>Rule</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980’s.</td>
<td>The Rule of 2 / 3</td>
<td>LMD, CABG&lt;br&gt;- Moderate &lt; LVEF&lt;br&gt;- Severe Ischemia&lt;br&gt;- 3 Vessel Disease&lt;br&gt;2vd + pLAD&lt;br&gt;Severe - Yes, STICH&lt;br&gt;Moderate - COURAGE OMT&lt;br&gt;ISCHEMIA&lt;br&gt;2vd in DM</td>
</tr>
<tr>
<td>1990’s.</td>
<td>The Rule of 2 / 3</td>
<td>PCI ?</td>
</tr>
<tr>
<td>2000’s</td>
<td>PCI &lt;, CABG &gt; (DM), Microc., OMT</td>
<td></td>
</tr>
<tr>
<td>2020’s</td>
<td>Anatomical, Isch.Score, Microc.: Ninv. - OMT+</td>
<td></td>
</tr>
</tbody>
</table>
CABG & OMT Evolving Again?

Microcirculation & OMT+Adherence

New York, Dec 9, 2016  No Disclosures
Untreated Lesions After FFR-Guided PCI: The Concept of Complete Revascularization

FAME (Y Kobayashi et. al.) JACC 2016;67:1701
One-year Event Rates For Continuous Body Mass Index According To Study Treatment

A Stroke or Systemic Embolism

B All-cause Mortality

C Stroke, Systemic Embolism, Myocardial Infarction or all-cause mortality

D Major bleeding

BMI: Q1:25.2, Median:28.5, Q3:32.5 kg/m²
HR (Solid Line) And 95% Confidence Interval (CI; Gray Area) For The Effect Of CABG Vs Medical Rx Across Ages

*STICH (MC Petrie et. al.) Circulation. 2016;134:1314*
Ten-Year Outcomes After CABG According to Age in Patients With HF and LV Systolic Dysfunction

STICH (MC Petrie et. al.) Circulation. 2016;134:1314
## Adjusted Hazard Ratio Plot Of Clinical And Safety Outcomes

### Primary FREEDOM Outcome
- **All-cause Mortality, MI, or Stroke**
  - DAPT: 12.5
  - SAPT: 16.0
  - p Value: 0.39

### Secondary Outcomes
- **All-cause Mortality**
  - DAPT: 5.8
  - SAPT: 9.4
  - p Value: 0.12
- **Vascular Mortality**
  - DAPT: 3.5
  - SAPT: 3.3
  - p Value: 0.72
- **Myocardial Infarction**
  - DAPT: 5.2
  - SAPT: 3.7
  - p Value: 0.40
- **Stroke**
  - DAPT: 3.2
  - SAPT: 4.1
  - p Value: 0.71
- **Cardiovascular Hospitalizations**
  - DAPT: 19.5
  - SAPT: 18.1
  - p Value: 0.62

### Primary Safety Outcomes
- **Major Bleeding**
  - DAPT: 5.6
  - SAPT: 5.7
  - p Value: 0.99
- **Blood Transfusions**
  - DAPT: 4.8
  - SAPT: 4.5
  - p Value: 0.82
- **Bleeding Hospitalization**
  - DAPT: 2.6
  - SAPT: 3.3
  - p Value: 0.74