Management of High-Risk Coronary Artery Disease

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Within the past 12 months, I have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Physician Name</th>
<th>Company/Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeffrey J. Popma, MD</td>
<td>Research Grants: Cordis, Boston Scientific, Abbott-Guidance, eV3</td>
</tr>
<tr>
<td></td>
<td>Medical Advisory Board: Cordis, Boston Scientific, Abbott Vascular</td>
</tr>
</tbody>
</table>
High-Risk PCI

- Defining High-Risk
  - Anatomic High Risk
  - Clinical Risk
- Choices for Revascularization
- High Anatomic and Surgical Risk
  - Hemodynamic Support
### Prior RCTs: “Two or Three Vessel Disease”

<table>
<thead>
<tr>
<th>Trial</th>
<th>Clinical Parameters</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mortality &amp; MI</td>
<td>Angina Relief</td>
<td>Repeat Revascularization</td>
<td></td>
</tr>
<tr>
<td>RITA2</td>
<td>No difference</td>
<td>PCI</td>
<td>PCI</td>
<td></td>
</tr>
<tr>
<td>ACME</td>
<td>No difference</td>
<td>PCI</td>
<td>PCI</td>
<td></td>
</tr>
<tr>
<td>MASS</td>
<td>No difference</td>
<td>PCI</td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td>AVERT</td>
<td>No difference</td>
<td>PCI</td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td>MASS II</td>
<td>No difference</td>
<td>PCI</td>
<td>No difference</td>
<td></td>
</tr>
<tr>
<td>COURAGE</td>
<td>No difference</td>
<td>No difference</td>
<td>No difference</td>
<td></td>
</tr>
</tbody>
</table>
Anatomic Risk Assessment Goes Well Beyond One-, Two-, or Three Vessel Disease
Quantitating Three Vessel Disease: SYNTAX Score

Local Heart team (surgeon & interventional cardiologist) assessed each patient in regards to:

- Patient’s operative risk (EuroSCORE & Parsonnet score)
- Coronary lesion complexity (newly developed SYNTAX score)
- The goal of the SYNTAX score is to provide a tool to assist physicians in their revascularization strategies for patients with high risk lesions

Sianos et al, EuroIntervention 2005;1:219-227
Valgimigli et al, Am J Cardiol 2007;99:1072-1081
Serruys et al, EuroIntervention 2007;3:450-459

Coronary tree segments based on the classification proposed by the AHA and modified for the ARTS study Circulation 1975; 51:31-3 & Semin Interv Cardiol 1999; 4:209-19

Leaman score, Circ 1981;63:285-299
Lesions classification ACC/AHA, Circ 2001;103:3019-3041
Bifurcation classification, CCI 2000;49:274-283
CTO classification, J Am Coll Cardiol 1997;30:649-656
SYNTAX Score: Selection Based on Anatomy

Patient 1
- LCx 70–90%
- LAD 70–90%
- RCA2 70–90%
- RCA3 70–90%
SYNTAX SCORE 21

Patient 2
- LM 99%
- LAD 99%
- LCx 100%
- RCA 100%
SYNTAX SCORE 54.5
Defining High-Risk
- Anatomic High Risk
- Clinical Risk

Choices for Revascularization

High Anatomic and Surgical Risk
- Hemodynamic Support
We Rarely Calculate Clinical Risk – But Are Often Left with Inoperable Patients Based on Surgical “Eyeball” Assessment
High-Risk PCI

- Defining High-Risk
  - Anatomic High Risk
  - Clinical Risk
- Choices for Revascularization
- High Anatomic and Surgical Risk
  - Hemodynamic Support
2009 ACC-SCAI Appropriateness Criteria


Endorsed by the American Society of Echocardiography, the Heart Failure Society of America, and the Society of Cardiovascular Computed Tomography

Coronary Revascularization Writing Group

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Patel et al JACC 2009 53 (February): 530-553
Coronary revascularization is appropriate when the expected benefits in terms of survival and health outcomes (symptoms, functional status, and/or quality of life) exceed the expected negative consequences of the procedure.
### Appropriateness: PCI vs CABG

<table>
<thead>
<tr>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No diabetes and normal LVEF</strong></td>
<td><strong>No diabetes and normal LVEF</strong></td>
</tr>
<tr>
<td>Two vessel coronary artery disease with proximal LAD stenosis</td>
<td>A</td>
</tr>
<tr>
<td>Three vessel coronary artery disease</td>
<td>A</td>
</tr>
<tr>
<td>Isolated left main stenosis</td>
<td>A</td>
</tr>
<tr>
<td>Left main stenosis and additional coronary artery disease</td>
<td>A</td>
</tr>
</tbody>
</table>

Patel et al JACC 2009 53 (February): 530-553
CONCLUSIONS

CABG remains the standard of care for patients with three-vessel or left main coronary artery disease, since the use of CABG, as compared with PCI, resulted in lower rates of the combined end point of major adverse cardiac or cerebrovascular events at 1 year. (ClinicalTrials.gov number, NCT00114972.)
The lowest and middle SYNTAX Terciles had similar outcomes between PCI and CABG.

- **SYNTAX Score ≤22**: P = 0.71
- **SYNTAX Score 23-32**: P = 0.10
- **SYNTAX Score ≥33**: P < 0.001

12-month MACCE, %:
- CABG (N=897): 14.4%
- TAXUS* (N=903): 13.5%
Health Related Quality of Life and U.S. Economic Outcomes of PCI with Drug-Eluting Stents vs. Bypass Surgery: 1-Year Results from the SYNTAX Trial

David J. Cohen, Tara A. Lavelle, Patrick W. Serruys, Friedrich W. Mohr, Haiyan Li, Yang Lei, Kajjun Wang, Kate Robertus, Elizabeth M. Mahoney, Yueping Zhu, Keith D. Dawkins, A. Pieter Kappetein on behalf of the SYNTAX Investigators
Primary QOL Endpoint:
SAQ–Angina Frequency

Δ = +1.3
P=0.17

Δ = -1.7
P=0.04

Δ = -1.7
P=0.03
SYNTAX: SAQ Subscales

SAQ-Physical Limitations
- Baseline: P<0.001
- 1 month: P=0.14
- 6 months: P=0.28

SAQ-Quality of Life
- Baseline: P<0.001
- 1 month: P=0.16
- 6 months: P=0.03

SAQ-Treatment Satisfaction
- PCI: P<0.001
- CABG: P=0.85
Cost-Effectiveness of CABG vs. PCI ($/QALY)
SYNTAX Score Tertiles

Low (≤22)

- Δ Cost: $6154
- Δ QALY: -0.047
- ICER: Dominated

Pr <$50K/QALY = 0.0%

Mid (23-32)

- Δ Cost: $3889
- Δ QALY: -0.013
- ICER: Dominated

Pr <$50K/QALY = 0.3%

High (≥33)

- Δ Cost: $467
- Δ QALY: +0.010
- ICER: $43,000/QALY

Pr <$50K/QALY = 49%
Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

Authors/Task Force Members: William Wijns (Chairperson) (Belgium)*, Philippe Kolh (Chairperson) (Belgium)*, Nicolas Danchin (France), Carlo Di Mario (UK), Volkmar Falk (Switzerland), Thierry Folliguet (France), Scot Garg (The Netherlands), Kurt Huber (Austria), Stefan James (Sweden), Juhani Knuuti (Finland), Jose Lopez-Sendon (Spain), Jean Marco (France), Lorenzo Menicanti (Italy)
Miodrag Ostojic (Serbia), Massimo F. Piepoli (Italy), Charles Pirlet (Belgium), Jose L. Pomar (Spain), Nicolaus Reifart (Germany), Flavio L. Ribichini (Italy), Martin J. Schalij (The Netherlands), Paul Sergeant (Belgium), Patrick W. Serruys (The Netherlands), Sigmund Silber (Germany), Miguel Sousa Uva (Portugal), David Taggart (UK)
The ESC Guidelines have based many of the decisions for revascularization on the SYNTAX score and the completeness of revascularization.
Where SYNTAX Went Wrong

Long-Term Follow-up Is Needed
Average number of stents implanted in the SYNTAX trial is higher than any other contemporary stent studies versus CABG study.

Average Stent Length = 86.1±47.9 mm
Importance of Sidebranch Occlusion in NWQMI

TAXUS Express was associated with more sidebranch occlusion – an event that is worsened with longer stents. Liberte may be different.
### Table 11. Recommendations for PCI for Unprotected Left Main Coronary Artery Disease

<table>
<thead>
<tr>
<th>Year</th>
<th>Recommendation</th>
<th>2009 PCI Focused Update Recommendations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005 PCI Guideline, Section 6.3.4.</td>
<td>1. It is reasonable that patients undergoing PCI to unprotected left main coronary obstructions be followed up with coronary angiography between 2 and 6 months after PCI. <em>(Level of Evidence: C)</em></td>
<td></td>
<td>Deleted recommendation (no longer recommended).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 PCI Guideline, Section 5.1</td>
<td>1. PCI of the left main coronary artery with stents as an alternative to CABG may be considered in patients with anatomic conditions that are associated with a low risk of PCI procedural complications and clinical conditions that predict an increased risk of adverse surgical outcomes (21,138,139).* <em>(Level of Evidence: B)</em></td>
<td></td>
<td>New recommendation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 PCI Guideline, Sections 5.2, 5.3</td>
<td>1. PCI is not recommended in patients with [...] f. Left main disease and eligibility for CABG. <em>(Level of Evidence: C)</em></td>
<td></td>
<td>Modified recommendation (bullet “f” from Section 5.1 and bullet “e” from Sections 5.2. and 5.3. are no longer current; see 2009 Class IIb recommendation #1).</td>
</tr>
</tbody>
</table>

Kushner et al JACC 2009;54;2205-2241
Defining High-Risk
- Anatomic High Risk
- Clinical Risk

Choices for Revascularization

High Anatomic and Surgical Risk
- Hemodynamic Support
# Anatomy vs Morbidity Risk Stratification

## STS score vs SYNTAX score

<table>
<thead>
<tr>
<th>SYNTAX score</th>
<th>STS score</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>PCI</td>
<td>PCI</td>
<td>PCI</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>PCI</td>
<td>PCI ± Support</td>
<td>PCI &amp; Support</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>CABG</td>
<td>CABG</td>
<td></td>
<td>PCI &amp; Support Or No Options</td>
</tr>
</tbody>
</table>

**PROTECT II patients**
Patients Requiring Prophylactic Hemodynamic Support During Non-Emergent High Risk PCI on Unprotected LM/Last Patent Conduit and LVEF ≤ 35% OR 3 Vessel Disease and LVEF ≤ 30%

Primary Endpoint = 30-day Composite MAE* rate

Follow-up of the Composite MAE* rate at 90 days

*I Major Adverse Events (MAE): Death, Stroke/TIA, MI (>3xULN CK-MB or Troponin), Repeat Revasc, Cardiac or Vascular Operation of Vasc. Operation for limb ischemia, Acute Renal Dysfunction, Increase in Aortic insufficiency, Severe Hypotension, CPR/VT, Angio Failure
<table>
<thead>
<tr>
<th></th>
<th>SYNTAX (PCI arm, n=903)</th>
<th>PROTECT II (n=448)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean±SD)</td>
<td>65±10</td>
<td>67±11</td>
</tr>
<tr>
<td>Male (%)</td>
<td>76</td>
<td>82</td>
</tr>
<tr>
<td>DM (%)</td>
<td>26</td>
<td>52</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>32</td>
<td>68</td>
</tr>
<tr>
<td>CHF (%)</td>
<td>4</td>
<td>87</td>
</tr>
<tr>
<td>LVEF ≤ 30% (%)</td>
<td>1.3</td>
<td>92</td>
</tr>
<tr>
<td>Euroscore (Mean±SD)</td>
<td>4±3</td>
<td>18±18</td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>IABP (N=223)</td>
<td>Impella (N=224)</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Age</td>
<td>67±11</td>
<td>68±11</td>
</tr>
<tr>
<td>Gender-Male</td>
<td>81.2%</td>
<td>79.5%</td>
</tr>
<tr>
<td>History of CHF</td>
<td>83.4%</td>
<td>91.1%</td>
</tr>
<tr>
<td>Current NYHA (Class III / IV)</td>
<td>54.8%</td>
<td>58.1%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>50.7%</td>
<td>52.2%</td>
</tr>
<tr>
<td>Implantable Cardiac Defib.</td>
<td>31.1%</td>
<td>34.8%</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>28.7%</td>
<td>38.4%</td>
</tr>
<tr>
<td>LVEF</td>
<td>24.1±6.3</td>
<td>23.5±6.3</td>
</tr>
<tr>
<td>STS Mortality score</td>
<td>6±7</td>
<td>6±6</td>
</tr>
<tr>
<td>Not Surgical Candidate</td>
<td>64.1%</td>
<td>63.4%</td>
</tr>
</tbody>
</table>
Maximal Decrease in CPO on device Support from Baseline (in 0.01 Watts)

<table>
<thead>
<tr>
<th>Device</th>
<th>N</th>
<th>Maximal Decrease</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP</td>
<td>138</td>
<td>-14.2 ± 27</td>
<td>0.001</td>
</tr>
<tr>
<td>Impella</td>
<td>141</td>
<td>-4.2 ± 24</td>
<td></td>
</tr>
</tbody>
</table>
PROTECT II MAE Outcome
Pre-specified High Risk PCI Without Atherectomy Group

Per Protocol (N=374)

- 30% MAE
  - 30 day MAE: 42.4% (N=19) vs. 29.5% (N=183), p=0.009
  - 90 day MAE: 51.1% (N=19) vs. 35.9% (N=181), p=0.003

Log rank test, p=0.005

Per Protocol (N=374)

- 30% MAE
  - 30 day MAE: 51.1% (N=19) vs. 35.9% (N=181), p=0.003

Per Protocol = Patients that met all incl./ excl. criteria.
**PROTECT II MACCE**

Per Protocol Population, N=426

Log rank test, p=0.04

**Using 8xULN threshold for biomarkers or Q-wave for Peri-procedural MI (Stone et al Circulation 2001;104:642-647) and 2xULN threshold for biomarkers for Spontaneous MI (Universal MI definition)**
Is PCI beneficial for these patients?
NYHA Improvement Post PCI

$p<0.001$

Baseline

<table>
<thead>
<tr>
<th>Class</th>
<th>Baseline</th>
<th>90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Class II</td>
<td>31%</td>
<td>44%</td>
</tr>
<tr>
<td>Class III</td>
<td>45%</td>
<td>30%</td>
</tr>
<tr>
<td>Class IV</td>
<td>17%</td>
<td>18%</td>
</tr>
</tbody>
</table>

58% reduction in Class III, IV

N=223 patients with NYHA measurements available at baseline and 90 days
LVEF vs Outcomes

**LVEF**
- Mean [95% CI]
  - IABP
  - Impella
- p (time) <0.001
- p (interaction) =0.5

**90 day MACCE**
- IABP: 31.0%
- Impella: 22.1%
- N=21
- N=215
- p=0.023
- ↓ 29% MACCE

Do patients undergoing more extensive revascularization benefit from left ventricular support device than IABP support?

TCT-2011 Presentation

Range of Ischemia Zone Score = [0-11]
## Protect II: Angiography Characteristics

<table>
<thead>
<tr>
<th>Procedural Characteristics</th>
<th>IABP (N=211)</th>
<th>Impella (N=216)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of lesion tx</td>
<td>2.53±1.2</td>
<td>2.53±1.2</td>
<td>0.98</td>
</tr>
<tr>
<td>Average lesion length</td>
<td>29.6±21.9</td>
<td>31.4±22.1</td>
<td>0.413</td>
</tr>
<tr>
<td>% of patients with 3 or more stents</td>
<td>41.7%</td>
<td>51.2%</td>
<td>0.05</td>
</tr>
<tr>
<td>Pre PCI Syntax Score</td>
<td>30±14</td>
<td>30±13</td>
<td>0.89</td>
</tr>
<tr>
<td>Post PCI Syntax Score</td>
<td>15±13</td>
<td>15±13</td>
<td>0.88</td>
</tr>
<tr>
<td>Delta (Pre- Post) in Syntax Score</td>
<td>15±9</td>
<td>15±10</td>
<td>0.721</td>
</tr>
<tr>
<td>Pre PCI Ischemia zone score (n=396)</td>
<td>9±2</td>
<td>9±2</td>
<td>0.9</td>
</tr>
<tr>
<td>Post PCI Ischemia zone score (n=396)</td>
<td>4±3</td>
<td>4±3</td>
<td>0.9</td>
</tr>
<tr>
<td>Delta Ischemia zone change (Δ IZS)</td>
<td>4.7±2.7</td>
<td>4.4±2.8</td>
<td>0.237</td>
</tr>
</tbody>
</table>
Risks assessment involves both an assessment of anatomic and clinical risk factors.

When the clinical surgical risk is low and the anatomy is complex, CABG is preferred.

When the clinical risk is high – and the anatomic risk is low (SYNTAX < 32), PCI is preferred.

When the clinical and anatomic risks are both high and the patients requires revascularization, there is evidence to support the use of percutaneous support devices in these patients.