Unprotected Left Main Stenting: Patient Selection and Recent Experience

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S. Raffaele Hospital, Milan, Italy
AHA/ACC 2005 Guidelines
Left Main CAD

Class IIa (Level B)

• The use of PCI for pts with significant unprotected LMCA stenosis is a reasonable revascularization in patients not eligible for CABG and in carefully selected pts.

• 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 (Level C).

Smith et al Circulation 2005;113:156-175
<table>
<thead>
<tr>
<th>Study</th>
<th>Site(s)</th>
<th>Years</th>
<th>Pts</th>
<th>Stent</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al</td>
<td>Asan Medical Center, Seoul, Korea</td>
<td>2003-2004</td>
<td>102</td>
<td>SES</td>
<td>EF ≤ 40% excluded 71% bifurcation</td>
</tr>
<tr>
<td>Valgimigli et al</td>
<td>Erasmus Medical Center, Netherlands</td>
<td>2001-2003</td>
<td>95</td>
<td>SES or PES</td>
<td>Acute MI 66% bifurcation</td>
</tr>
<tr>
<td>Chieffo et al</td>
<td>Columbus and San Raffaele Hospital, Milan</td>
<td>2002-2004</td>
<td>85</td>
<td>SES or PES</td>
<td>45% poor surgical candidates and 81% bifurcation</td>
</tr>
<tr>
<td>Price et al</td>
<td>Scripps Clinic</td>
<td>2002-2004</td>
<td>51</td>
<td>SES</td>
<td>24% had EF ≤ 40% and 92% bifurcation</td>
</tr>
<tr>
<td>Lefevre et al*</td>
<td>Institute Cardiovasculare, France</td>
<td>2003-2004</td>
<td>130</td>
<td>PES</td>
<td>76% bifurcation</td>
</tr>
</tbody>
</table>
Left Main Stenting with DES

<table>
<thead>
<tr>
<th></th>
<th>Restenosis</th>
<th>Rivascularization</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price</td>
<td>44%</td>
<td>39%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Park</td>
<td>10%</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>(n=102)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valgimigli</td>
<td>6%</td>
<td>14%</td>
<td>0</td>
</tr>
<tr>
<td>(n=95)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chieffo</td>
<td>19%</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>(n=85)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lefevre</td>
<td>3.5%</td>
<td>4.2%</td>
<td>1.6%</td>
</tr>
<tr>
<td>(n=146)</td>
<td></td>
<td></td>
<td>1.5%</td>
</tr>
</tbody>
</table>
### 886±308 days Clinical Follow-Up

<table>
<thead>
<tr>
<th>Event</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n (%)</td>
<td>5  (3.4)</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>4  (2.7)</td>
</tr>
<tr>
<td>TLR, n (%)</td>
<td>1  (0.7)</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>7  (4.7)</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>0</td>
</tr>
<tr>
<td>MACE, n (%)</td>
<td>11 (7.4)</td>
</tr>
</tbody>
</table>

6-Month Angiographic Follow-Up

Angiographic Fup was performed in 106 (73%) of the pts

<table>
<thead>
<tr>
<th></th>
<th>n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restenosis, %</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Late Loss, mm</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

Drug Eluting stent for LeFT main (DELFT) Registry

Study population

April 2002 to April 2004

358 consecutive patients with de novo ULMCA disease

SES or PES

Meliga et al J Am Coll Cardiol. 2008 Jun 10;51(23):2212-9
# Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Diagnosis at admission</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable Angina</td>
<td>44.1%</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>41.9%</td>
</tr>
<tr>
<td><strong>AMI</strong></td>
<td>8.4%</td>
</tr>
<tr>
<td><strong>AMI+shock</strong></td>
<td>2.8%</td>
</tr>
<tr>
<td><strong>Silent Ischemia</strong></td>
<td>2.8%</td>
</tr>
</tbody>
</table>

| LVEF                           | 48.6±12.8 |
| EuroScore                      | 6.4±4.1   |

<table>
<thead>
<tr>
<th>Ratio</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;6</td>
<td>20.1%</td>
</tr>
<tr>
<td>&gt;9</td>
<td>31.0%</td>
</tr>
<tr>
<td>Elective</td>
<td>5.7±3.8</td>
</tr>
<tr>
<td>Emergent</td>
<td>9.9±3.5</td>
</tr>
</tbody>
</table>

**19.6% Emergent PCI**
DELFT
K-M survival analysis - Death + MI

Whole: 83.4%
Elec: 86%
Emerg: 72.6%
P=0.005

RR: 2.11
1.37 < RR < 3.2

RR: 1.68
0.42 < RR < 4.78

RR: 1.33
0.22 < RR < 7.8
Late and Very Late Stent Thrombosis Multicenter Registry

Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DES (n = 731)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>63.1±11.8</td>
</tr>
<tr>
<td><strong>Current or ex-smoker</strong></td>
<td>247 (33.8%)</td>
</tr>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
<td>368 (50.3%)</td>
</tr>
<tr>
<td><strong>Systemic hypertension</strong></td>
<td>427 (58.4%)</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td>176 (24.0%)</td>
</tr>
</tbody>
</table>

Chieffo et al Eur Heart J 2008 Jun 18
Lesion and Procedural Characteristics

Lesion Location

- Distal: 559 (76.5%)
- Ostium/Shaft: 172 (23.5%)

n = 731

Stent Type

- Taxus: 196 (26.8%)
- Cypher: 536 (73.3%)
Procedural Characteristics

Stent Technique

- Crush 120 (43)
- Culotte 24 (9)
- T-Stenting 52 (19)
- V-Stenting 80 (29)

Late and Very Late Stent Thrombosis Multicenter Registry

- n = 559
- Stent both branches 276 (49.4)
- Final Kissing Inflation 360 (64%)
## Late and Very Late Stent Thrombosis Multicenter Registry

### In-Hospital and Long Term Follow-up

<table>
<thead>
<tr>
<th>Event</th>
<th>In Hospital</th>
<th>Follow-up (29.5 ± 13.7 ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=731</td>
<td>n=726</td>
</tr>
<tr>
<td>Cardiac Death, n (%)</td>
<td>5 (0.7)</td>
<td>26 (3.6)</td>
</tr>
<tr>
<td>Total Death, n (%)</td>
<td>5 (0.7)</td>
<td>40 (5.5)</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>69 (9.4)</td>
<td>11 (1.5%)</td>
</tr>
<tr>
<td>TLR, n (%)</td>
<td>2 (0.3)</td>
<td>76 (10.5)</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>2 (0.3)</td>
<td>95 (13.0)</td>
</tr>
<tr>
<td>MACE, n (%)</td>
<td>73 (9.9%)</td>
<td>138 (19.0)</td>
</tr>
</tbody>
</table>

*Chieffo et al Eur Heart J 2008 Jun 18*
### Stent Thrombosis ARC Definitions

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite Stent Thrombosis</td>
<td>4</td>
<td>0.54%</td>
</tr>
<tr>
<td>Probable Stent Thrombosis</td>
<td>3</td>
<td>0.4%</td>
</tr>
<tr>
<td>Possible Stent thrombosis</td>
<td>20</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

*Late thrombosis in a Taxus stent in LAD at 3 ms

Chieffo et al. Eur Heart J 2008 Jun 18
GISE-SICI survey on Left Main Stenting
n = 1,453 patients, 19 Italian Centers

Courtesy of Prof. Tamburino
Overall mortality: DES 85.8% vs 72.2%
Adjusted HR 0.40 (95% CI 0.25-0.63)

Cardiac mortality: DES 90.8% vs 81.0%
Adjusted HR 0.32 (95% CI 0.19-0.55)

GISE Registry DES vs BMS

MI and TLR

DES 91.0% vs. 80.3% BMS

DES 83.6% vs 76.7% BMS

GISE Registry DES vs BMS
Ostium and shaft subanalysis - 3 years outcome

Overall mortality - unadjusted

Cardiac mortality - unadjusted

P < 0.001

P = 0.015

Tamburino, et al. Eur Heart J 2009 Ahead of print
GISE Registry DES vs BMS
Ostium and shaft subanalysis - 3 years outcome

TLR-free survival (%)

MACE-free survival (%)

Log-rank Test = 0.20
Log-rank Test = 0.002

TLR - unadjusted
MACE-unadjusted

P = 0.20
P = 0.002

ISAR Left Main
Primary Endpoint: 1-Year MACE

RR 0.85; 95% CI 0.56 to 1.29

Pre-specified margin 8%

Difference in MACE

On Courtesy of Dr Mehilli
Milan Experience CABG vs. DES

Cumulative MACCE at 1 Year

PCI better
n=107

CABG better
n=142

OR and Exact 95% CI

Milan Experience CABG vs. DES

CVE+MI+Death at 1 Year

PCI better
n=107

CABG better
n=142

OR and Exact 95% CI
Milan Experience CABG vs. DES

MACCE at 4 years
(including repeated revascularization)

Odds Ratio and Exact 95% CI

36% in DES vs 28% in CABG
Adjusted OR 1.44  (95% CI 0.75 -2.77;P=0.30)
**Milan Experience CABG vs. DES**

**CVE+Death+MI at 4 years**

Odds Ratio and Exact 95% CI

- Total Population: 249
- PROPENSITY SCORE:
  - 1st Quartile: 63
  - 2nd Quartile: 61
  - 3rd Quartile: 62
  - 4th Quartile: 63

14% in DES vs 22% in CABG

Adjusted OR = 0.43 (0.17 - 0.97; P = 0.04)
MAIN-COMPARE Study
Stenting (BMS or DES) vs. CABG

Wave I
- LMCA disease
  - BMS (N=318)
  - CABG (N=448)

Wave II
- LMCA disease
  - DES (N=784)
  - CABG (N=690)

Total (N=2240)
- PCI (N=1102)
- CABG (N=1138)

Death

(Overall PCI and CABG matched cohort: 542 pairs)

Target-vessel revascularization

(Overall PCI and CABG matched cohort: 542 pairs)

71% enrolled (N=3,075) All Pts with de novo 3VD and/or LM disease (N=4,337)

Treatment preference
- Referring MD or pts. refused informed consent (7.0%)
- Inclusion/exclusion (4.7%)
- Withdrew before consent (4.3%)
- Other (1.8%)
- Medical treatment (1.2%)

PCI n=198
CABG n=1077
TAXUS* n=903
CABG n=897

5yr f/un=649
vs
2500 w/ f/u

Total enrollment N=3075
Stratification: LM and Diabetes

Randomized Arms
N=1800
- CABG N=897
  - DM 28.5%
  - Non DM 71.5%
- TAXUS* N=903
  - DM 28.2%
  - NonDM 71.8%

Amenable for both treatment options

Two Registry Arms
N=1275
- CABG N=1077
- PCI N=198

Amenable for only one treatment approach

Stratification: LM and Diabetes

23 US Sites
62 EU Sites

Heart Team (surgeon & interventionalist)

23 US Sites
62 EU Sites

Amenable for both treatment options

Amenable for only one treatment approach

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62 EU Sites

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62 EU Sites

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23 US Sites
62 EU Sites

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- CABG N=897
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Amenable for both treatment options

Two Registry Arms
N=1275
- CABG N=1077
- PCI N=198

Amenable for only one treatment approach

23 US Sites
62 EU Sites

Heart Team (surgeon & interventionalist)
MACCE to 12 Months
Left Main Subset

CABG (N=348)  TAXUS (N=357)

Cumulative Event Rate (%)

Months Since Allocation

Event rate ± 1.5 SE, *Fisher exact test  ITT population

P=0.44*
Death/CVA/MI to 12 Months

SYNTAX Left Main Subset

CABG (N=348)

TAXUS (N=357)

P=0.29

Cumulative Event Rate (%)

9.1%

7.0%

Months Since Allocation

Event rate ± 1.5 SE, *Fisher exact test

ITT population
Symptomatic Graft Occlusion & Stent Thrombosis to 12 Months

Left Main Subset

CABG (n=348)  TAXUS (n=357)

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>n=11</th>
<th>n=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>TAXUS</td>
<td>2.7</td>
<td></td>
</tr>
</tbody>
</table>

P = 0.49
MACCE to 12 Months by SYNTAX Score Tertile

High Scores (≥33) Left Main Subset

<table>
<thead>
<tr>
<th>SYNTAX Score</th>
<th>Mean baseline (± SE)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>42.1 ± 7.6</td>
<td>0.008*</td>
</tr>
<tr>
<td>TAXUS</td>
<td>43.8 ± 9.1</td>
<td></td>
</tr>
</tbody>
</table>

Event rate ± 1.5 SE, *Fisher exact test
### Overall MACCE at 12 Months
#### Left Main Subset

<table>
<thead>
<tr>
<th>Subset</th>
<th>CABG (%)</th>
<th>TAXUS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LM all (n=705)</td>
<td>13.7</td>
<td>15.8</td>
</tr>
<tr>
<td>LM only (n=91)</td>
<td>8.5</td>
<td>7.1</td>
</tr>
<tr>
<td>LM+1VD (n=138)</td>
<td>13.2</td>
<td>7.5</td>
</tr>
<tr>
<td>LM+2VD (n=218)</td>
<td>14.4</td>
<td>19.8</td>
</tr>
<tr>
<td>LM+3VD (n=258)</td>
<td>15.4</td>
<td>19.3</td>
</tr>
</tbody>
</table>

**P-values:**
- LM all: $P=0.44$
- LM only: $P=1.0$
- LM+1VD: $P=0.27$
- LM+2VD: $P=0.29$
- LM+3VD: $P=0.42$
Conclusions I

- PCI on unprotected LMCA lesions should be performed electively by experienced interventional operators in selected institutions.

- At present, patients should be fully informed of the potential risks of the procedure in the context of limited data.
Conclusions II

- Careful patient and lesion selection is necessary in percutaneous treatment of unprotected LMCA.

- Conclusive information about the optimal treatment of LMCA will come only from prospective, randomized trial comparing CABG vs PCI with extended follow-up at least until 5 years.