PCI in Diabetes

Δημήτριος Συρσελούδης
Επιμελητής Καρδιολογίας
PREVALENCE OF CAD IN DM %

DM IN PCI PTS %

DM IN CABG PTS %

DM INPTS W ACS %

55

15-25

40

25-30

G. Kassimis HJC 2017; T. Hammoud JACC 2000; T. Lüscher Circulation 2003
DM and CAD

NCEP ATPIII

DM is accorded a CAD risk equivalent

PREVALENCE OF CAD IN DM %

DM IN PTS W ACS %
DM and CAD prognosis

- CAD in DM:
  Death rate = 45% over 7 yrs and 75% over 10 yrs

- MI in DM:
  death rate= ~ 50% over 5 yrs
  — J. Herlitz, Diabet Med 1998

- OASIS registry:
  DM increased mortality in UA by 57%
  — K. Maimberg, Circulation 2000

- SHOCK trial:
  DM increased mortality in cardiogenic shock post MI by 36%
  — DM Shindler JACC 2000
Diabetic traits compromising PCI

Medial calcification mediated by glycosylation process TCFAs with spontaneous plaque rupture

FoxO transcription factors targets of insulin and GF signaling (cell size, function, metabolism). Activation is associated with myocardial dysfunction in CAD

Hyperphosphatemia & macrophage derived matrix vesicles associated with medial calcification

Insulin triggers the macrophage release of proinflammatory mediators: TNF-a, IL-1b etc

Lower levels of clopidogrel active metabolites

Altered antiplatelet pharmacokinetics

DM and CAD anatomic characteristics

Table 5. Angioscopic Findings in Diabetic and Nondiabetic Patients

<table>
<thead>
<tr>
<th></th>
<th>Diabetic Patients (n=77)</th>
<th>Nondiabetic Patients (n=38)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque color</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow</td>
<td>15 (88%)</td>
<td>32 (84%)</td>
<td>NS</td>
</tr>
<tr>
<td>White</td>
<td>2 (12%)</td>
<td>6 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>Plaque surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rough</td>
<td>15 (88%)</td>
<td>26 (68%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ulceration</td>
<td>16 (94%)</td>
<td>23 (60%)</td>
<td></td>
</tr>
<tr>
<td>Thrombus</td>
<td>16 (94%)</td>
<td>21 (55%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Macrophage infiltration

Necrotic core, calcium

Ulceration, Thrombi

In patients with diabetes, the indications for myocardial revascularization are the same as those in patients without diabetes (see sections 5, 6, and 7).
**PCI vs MT**

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>No. of Patients</th>
<th>Hazard Ratio (95% CI)</th>
<th>Event Rate for the Primary Outcome</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>Medical Therapy</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>Yes</td>
<td>766</td>
<td>0.99 (0.73–1.32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1468</td>
<td>1.20 (0.92–1.56)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Courage Trial**

2287 patients, f/u 4.6 yrs
PCI group 1149 – medical-therapy group 1138

**BARI 2D Trial PCI Stratum**

PCI group 798 – medical-therapy group 807
5 yrs f/u

PCI vs CABG

**Freedom Trial**: PCI 953, CABG 947, 5 yrs f/u

**CARDia**: PCI 254, CABG 256, 1 yr f/u

Kaplan – Meier estimates of outcomes 2 and 5 yrs post randomization- FREEDOM

<table>
<thead>
<tr>
<th>Outcome</th>
<th>2 Years after Randomization</th>
<th>5 Years after Randomization</th>
<th>Patients with Event</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCI</td>
<td>CABG</td>
<td>PCI</td>
<td>CABG</td>
</tr>
<tr>
<td>number (percent)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary composite†</td>
<td>121 (13.0)</td>
<td>108 (11.9)</td>
<td>200 (26.6)</td>
<td>146 (18.7)</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>62 (6.7)</td>
<td>57 (6.3)</td>
<td>114 (16.3)</td>
<td>83 (10.9)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>62 (6.7)</td>
<td>42 (4.7)</td>
<td>98 (13.9)</td>
<td>48 (6.0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>14 (1.5)</td>
<td>24 (2.7)</td>
<td>20 (2.4)</td>
<td>37 (5.2)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>9 (0.9)</td>
<td>12 (1.3)</td>
<td>73 (10.9)</td>
<td>52 (6.8)</td>
</tr>
</tbody>
</table>

**ALL MORTALITY:** UNDERPOWERED  
**COMPOSITE END POINT:** LED BY NON Q WAVE MYOCARDIAL INFARCTION  
**STROKE:** MORE IN CABG  
**CARDIOVASCULAR DEATH:** NO DIFFERENCE

Farkouh, NEJM 2012
All cause mortality – Extended follow up cohort

HR (95% CI): 1.32 (0.97, 1.78)
P = 0.07 by log-rank test

- PCI: 23.7%
- CABG: 18.7%

Farkouh, J Am Coll Cardiol 2018
All cause mortality – Whole FREEDOM cohort

- Survival
- Mortality

"n = 1900 patients"

HR (95% CI): 1.36 (1.07, 1.74)
P = 0.01 by log-rank test

- PCI 24.3%
- CABG 18.3%
PCI vs CAGB

SYNTAX diabetics (n=452)
CABG: 221; PCI: 231, 5yrs F/U

Death/Stroke/MI
23.9% vs 19.1%, p=NS

Repeat Revasc
35.3% vs 14.6%, p<0.001
DM was NOT an independent mortality predictor and therefore it was excluded from SYNTAX SCORE II.
PCI vs CABG

BEST trial: EES vs CABG (n=880)
CABG:442 ; PCI : 438, 4.6 yrs F/U

SJ Park; N Engl J Med 2015
3052 patients compared PCI with the use of early-generation DES vs. CABG
Higher risk for Death/MI
Lower risk for Stroke in PCI
Mortality risk in CABG vs PCI in diabetics with MVD metanalysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Events PCI Total</th>
<th>Events CABG Total</th>
<th>Odds Ratio OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARI</td>
<td>47 173</td>
<td>16 180</td>
<td>3.82</td>
<td>[2.07; 7.06]</td>
</tr>
<tr>
<td>ARTS</td>
<td>15 112</td>
<td>8 96</td>
<td>1.70</td>
<td>[0.69; 4.21]</td>
</tr>
<tr>
<td>ERACI II</td>
<td>4 39</td>
<td>4 39</td>
<td>1.00</td>
<td>[0.23; 4.32]</td>
</tr>
<tr>
<td>MASS II</td>
<td>9 56</td>
<td>9 59</td>
<td>1.06</td>
<td>[0.39; 2.91]</td>
</tr>
<tr>
<td>SoS</td>
<td>7 68</td>
<td>1 74</td>
<td>8.38</td>
<td>[1.00; 69.98]</td>
</tr>
<tr>
<td>CARDia</td>
<td>37 254</td>
<td>32 248</td>
<td>1.15</td>
<td>[0.69; 1.92]</td>
</tr>
<tr>
<td>SYNTAX</td>
<td>44 226</td>
<td>26 202</td>
<td>1.64</td>
<td>[0.97; 2.77]</td>
</tr>
<tr>
<td>VA CARDS</td>
<td>21 101</td>
<td>5 97</td>
<td>4.83</td>
<td>[1.74; 13.40]</td>
</tr>
<tr>
<td>FREEDOM</td>
<td>114 699</td>
<td>83 761</td>
<td>1.59</td>
<td>[1.17; 2.16]</td>
</tr>
</tbody>
</table>

Fixed effect model

Random effects model

Heterogeneity: $I^2$-squared=52.2%, $\tau^2$-squared=0.1228, $p=0.033$
## SURVIVAL BENEFIT IN DIABETICS WITH STABLE DISEASE SUITABLE FOR REVASCULARIZATION EITHER WITH CABG OR WITH PCI

<table>
<thead>
<tr>
<th></th>
<th>PCI better than MT for Survival</th>
<th>CABG better than MT for Survival</th>
<th>CABG or PCI better than MT for Survival</th>
<th>Equivalence of CABG and PCI for Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>No benefit</td>
<td>BARI 2D</td>
<td>BARI 2D</td>
<td>PCI better: None</td>
<td></td>
</tr>
</tbody>
</table>
WHICH DIABETIC SHOULD GET PCI FOR STABLE DISEASE?

• Revascularization for symptoms:
  – Ischemic symptoms under optimal MT
  – Low SYNTAX score \( \leq 22 \) (mainly focal disease)
DM + ACS + focal disease: early revascularization with PCI

DM + ACS + MVD should probably:
1. urgent or emergency PCI for the culprit lesion
2. Heart Team consultation: MT, PCI, or CABG for the remaining significant obstructive CAD

extensive MVD, +/- proximal LAD + a left internal mammary graft usabe: CABG is preferred
GLYCEMIC CONTROL

1,850 FREEDOM subjects
DM + MVD, MACE (death, MI, or stroke) rate is higher in patients treated with insulin

CABG was superior to PCI/DES in both DM types and the magnitude of treatment effect was similar

G. Dangas, J Am Coll Cardiol 2014
Tight glycemic control was unhelpful or associated with increased cardiovascular events.

**NO STUDIES TO ASSOCIATE PCI OUTCOME WITH GLYCEMIC CONTROL**


Effects of prandial versus fasting glycemia on cardiovascular outcomes in type 2 diabetes: the HEART2 trial.

VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes.


UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34).
Insulin sensitization with metformin (74.6%) or a thiazolidinedione (62.1%) did not improve the primary end point of freedom from major cardiovascular events.

Insulin sensitization vs insulin provision group: 77.7% vs 75.4%; P=0.13
it is generally recommended that in elective cases, metformin should be withheld before angiography or PCI for 48 h

However, clinical experience suggests that the actual risk of lactate acidosis is very small and therefore

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended to check renal function if patients have taken metformin immediately before angiography and withhold metformin if renal function deteriorates.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

arterial pH <7.35, blood lactate >5 mmol/L (45 mg/dL), and detectable plasma metformin concentration should prompt the initiation of haemodialysis
• Current evidence suggests that DM impair the response to PCI and CABG appears to be better especially in complex disease
• A revascularization procedure is only one component of a comprehensive strategy involving also cardiac rehabilitation, and strict risk factor control.
• We are still missing the links between the metabolic derangements and the clinical manifestations of DM that render PCI a less suitable option for CAD treatment in diabetics.