PCI IN DIABETIC PATIENT

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Euromedica ‘Kyanous Stavros, THESSALONIKI
Revascularisation in Diabetes Mellitus

• Heartwire (www.theheart.org) Nov 1999
  • “Despite stents, diabetic patients undergoing PCI still face higher death rates.”

• AHA Scientific Statement 1999
  • “Recent studies indicate that coronary angioplasty is less efficacious for patients with diabetes than for those without; these reports further reveal that CABG is the preferred therapy in patients with diabetes when invasive management is required.”
Recommendations for 2007:
Which diabetic patients should undergo PCI?

- Single-vessel disease
- No evidence of involvement of proximal or mid-LAD (i.e., no LIMA)
- Patients with 2 or 3 highly discrete lesions without evidence of diffuse atherosclerosis (i.e., “low risk”)
- Patients with important contraindications to CABG
  - Previous CABG with patent LIMA
  - Advanced age
The Problem

- At least 65 percent of people with diabetes mellitus die of some form of heart disease or stroke.
  - Versus < 50% of those without DM
  - Often the death is at an earlier age

- Heart disease death rates among adults with diabetes are two to four times higher than the rates for adults without diabetes.

NIDDK/NIH, (diabetes.niddk.nih.gov)
Diabetic Vascular Pathology

- ↑ plasma coagulation
- Altered response to arterial injury
- Diminished fibrinolysis
- ↓ endothelial thromboresistance
- Platelet hyperreactivity (diabetic thrombocytopenia)
- ↑ platelet aggregation and adhesion

Features of DM promote risk for ACS

- Prothrombotic
- Proinflammatory states,
- Endothelial dysfunction
- Metabolic disorders
  - hyperglycaemia,
  - dyslipidaemia,
  - obesity,
  - insulin resistance
  - Oxidative stress,

Purported mechanisms that contribute to increased platelet aggregation in DM

- Hyperglycaemia
  - May induce the expression of the surface adhesion molecule P-selectin,
  - Promotes glycation of platelet surface proteins
    - Consequent decrease in membrane fluidity
    - Platelet adhesion increase,
  - Activation of protein kinase C,
  - Possible direct osmotic effects
  - Promotes atherothrombosis
    - Oxidation of amino groups,
    - Formation of advanced glycation endproducts,
    - Endothelial dysfunction,
    - Subendothelial cellular proliferation,
    - Increased matrix expression

Purported mechanisms that contribute to increased platelet aggregation in DM

- Potential mechanisms of drug resistance
  - Increased expression of the platelet receptor glycoprotein (GP) IIb/IIIa
  - Up-regulation of platelet P2Y12 receptor signalling (theinopyridines)
  - Increased platelet turnover (ASA)

- Other metabolic conditions
  - obesity via insulin resistance
    - may increase intracellular calcium concentration
    - May impair the response to nitric oxide.
  - augmented cytosolic calcium concentration,
  - increased oxidative stress)
  - dyslipidaemia,
  - systemic inflammation
  - endothelial dysfunction

ACS mortality in patients with DM

Figure 3. Cumulative Incidence of All-Cause Mortality Through 1 Year After ACS

Donahoe, JAMA 2007
Trends in post ACS mortality and DM

Early mortality of diabetic and non-diabetic patients with acute myocardial infarction: Historical perspective

- Pre CCU era (<1962)
- CCU era (1962–1984)
- Primary PCI (since 1996)

Soler et al. Lancet 1974
Barbash et al. JACC 1993
Kagawa et al. Am J Cardiol 2007

Radke et al. European Heart Journal 2010
Acute STE MI approaches

- Meta-analysis of the Fibrinolytic Therapy Trialists’ Collaborative Group I
  - 21,659 subjects 2236 of whom were diabetic
  - greater than twofold survival benefit at 35 days among diabetic patients
    - corresponding to 3.7 lives for those with DM and 1.5 lives saved in those without DM per 100 patients treated.

- Primary PCI
  - 367 diabetic patients enrolled in 11 randomised trials
  - Primary PCI had lower event rates (9.2% vs. 19.3%, p <0.05).
  - Overall, the benefit of primary PCI over thrombolytic therapy was greater in diabetic patients compared with non-diabetic patients (number needed-to-treat [NNT] 10 and 16, respectively).
Revasc after ACS - Euro Heart Study

- 3488 patients 2/3 with unstable CAD followed for 1 year
  - 2063 non-DM
  - 1425 DM

- Revascularization was of no benefit in non-DM patients but DM patients with significant reductions in
  - Mortality (5.7 vs. 8.6%)
  - Composite of death, MI, or stroke (9.9 vs. 16.9%)

- Significant interaction between DM status and effect of revasc

- Drove European guidelines to recommend an early invasive strategy for all DM patients presenting with ACS

Impact of Diabetes on Outcomes After PCI With DES in Relation to CAD Complexity

Pooled analysis of 6,081 patients from 4 all-comers trials that included use of newer-generation DES in 75% and analysis by SYNTAX score.

<table>
<thead>
<tr>
<th>Outcomes at 2 Years:</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes vs No Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>1.25</td>
<td>1.03-1.53</td>
</tr>
<tr>
<td>TLR</td>
<td>1.54</td>
<td>1.18-2.01</td>
</tr>
<tr>
<td>TVR</td>
<td>1.38</td>
<td>1.08-1.76</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>1.41</td>
<td>0.96-2.07</td>
</tr>
<tr>
<td>MI</td>
<td>0.89</td>
<td>0.64-1.22</td>
</tr>
</tbody>
</table>

**Conclusion:** Diabetic patients are at higher risk for repeat procedures and MACE than nondiabetic patients after PCI, regardless of disease complexity.


The Source for Interventional Cardiovascular News and Education
BARI 2 D

- 2368 subjects presenting for evaluation of coronary disease randomized to medical therapy vs revascularization and to either insulin sensitization or insulin provision therapy in a 2x2 manner

- At 5 years no survival benefit with prompt revascularization

- There was reduction in subsequent MI only for those undergoing coronary artery bypass as revascularization (22.4% vs 32.5%). Most of this benefit was in the cohort receiving insulin.

BARI Study Group NEJM 2009
Diabetes and Clopidogrel-Induced Antiplatelet Effects

Loading Phase of Treatment

- **DM**: 38% (P = 0.04)
  - 8% Non-responders (Platelet inhibition < 10%)
  - 14% Low responders (Platelet inhibition 10-29%)
  - 56% Responders (Platelet inhibition ≥ 30%)

- **No DM**: 6% (78%)

24h post 300 mg LD

Maintenance Phase of Treatment

- **ADP 20 μmol/L**
  - T2DM: 62.9 ± 0.1
  - No DM: 43.0 ± 0.1
  - **P = 0.001**

- **ADP 6 μmol/L**
  - T2DM: 41.5 ± 0.1
  - No DM: 31.8 ± 0.1
  - **P < 0.0001**

Platelet Aggregation (%)

ADP = Adenosine Diphosphate; DM = Diabetes Mellitus; LD = Loading Dose; MD = Maintenance Dose; T2DM = Type 2 Diabetes Mellitus

1 Angiolillo DJ et al. *Diabetes* 2005;54:2430-2435
2 Angiolillo DJ et al. *J Am Coll Cardiol* 2006;48:206-304
CV thrombotic Events by Diabetic Status

- No Diabetes (N=10,462)
- Diabetes (N=3,146)

Event Rate, %

- Mortality: 6.9% (No Diabetes), 13.0% (Diabetes)
- CVD/MI/CVA: 9.9% (No Diabetes), 14.6% (Diabetes)
- New MI: 7.5% (No Diabetes), 10.7% (Diabetes)
- Stent Thrombosis: 1.4% (No Diabetes), 2.8% (Diabetes)

P<0.001 for all categories

CVD=Cardiovascular Death, MI=Myocardial Infarction, CVA=Stroke

Subgroup of Patients with Diabetes: LD Phase - Platelet Function Measures

![Graph showing platelet function measures for different time points and treatment groups.](image)
Subgroup of Patients with Diabetes: MD Phase - Platelet Function Measures

All ACS Population & Diabetic Subgroup: Primary End Point

*Primary End Point: CV Death, NMI, or NF Stroke. Inclusive of diabetic subgroup. Cumulative Kaplan-Meier estimates of the rates of key study end points during the follow-up period. ACS=Acute Coronary Syndrome; ARR=Absolute Risk Reduction; CV=Cardiovascular; DM=Diabetes Mellitus; HR=Hazard Ratio; MI=Myocardial Infarction; NF=Nonfatal; NNT=Number Needed to Treat

Wu et al. NEJM 2007 357 2001-2015
Adapted from Antman et al. American Heart Association Scientific Sessions 2007, Nov 4-7; Orlando, FL
## Diabetic Subgroup: Primary End Point Reduction

(CV Death, NF MI or NF Stroke)

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel Prasugrel Reduction in Risk (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DM (n = 10,462)</td>
<td>10.6, 9.2, 14</td>
<td>0.02</td>
</tr>
<tr>
<td>All DM (n = 3,146)</td>
<td>17.0, 12.2, 30</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>DM No Insulin (n = 2,370)</td>
<td>15.3, 11.5, 26</td>
<td>0.009</td>
</tr>
<tr>
<td>DM On Insulin (n = 776)</td>
<td>22.2, 14.3, 37</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Inulin therapy was identified at time of randomization.
CV = Cardiovascular; DM = Diabetes Mellitus; HR = Hazard Ratio; MI = Myocardial Infarction; NF = Nonfatal

Wiviott SD et al. Circulation 2009; 119: 1826-1836
Patients With Diabetes vs Patients Without Diabetes: Stent Thrombosis (ARC Definite or Probable)

HR 0.52 (0.33-0.84) P = 0.007
Clopidogrel 3.6
Prasugrel 2.0

HR 0.45 (0.31-0.65) P < 0.001
Clopidogrel 2.0
Prasugrel 0.9

P interaction = 0.63. Cumulative Kaplan-Meier estimates of the rates of key study end points during the follow-up period.
ARC=Academic Research Consortium; DM=Diabetes Mellitus; HR=Hazard Ratio
Bivard SD et al. Circulation 2008;118:1526-1536

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Non-CABG TIMI Major or Minor Bleeding in Patients With Diabetes

- **Non-CABG TIMI Major\(^1\) or Minor\(^2\) Bleeding**
  - **All-ACS\(^1\)**: Prasugrel 3.4, Clopidogrel 4.5
  - **Diabetes\(^3\)**: Prasugrel 3.8, Clopidogrel 4.9

- **Non-CABG TIMI Major Bleeding**
  - **All-ACS\(^1\)**: Prasugrel 1.7, Clopidogrel 2.2
  - **Diabetes\(^3\)**: Prasugrel 2.2, Clopidogrel 2.3

\(^1\)Observed event rates.
\(^2\)Intracranial hemorrhage or clinically overt bleeding associated with a fall in hemoglobin ≤5 g/dL.
\(^3\)Clinically overt bleeding associated with a fall in hemoglobin ≥3 g/dL but <5 g/dL.

\(^5\)Value not provided due to sample size limitations.

1. Efficacy Full Prescribing Information.
Ticagrelor

- First in class cyclopentyltriazolopyrimidine,
  - direct-acting (i.e. no metabolism is required) oral agent and
  - reversible P2Y12 inhibitor
  - more prompt and potent platelet inhibitory effects than clopidogrel.

**PLATO (Platelet Inhibition and Patient Outcomes) - 18624 ACS**

- ticagrelor compared with clopidogrel (300–600 mg) loading
- Composite endpoint of death from vascular causes, MI or stroke at 12 months
  - Primary outcome (10.2 vs. 12.3%; HR = 0.84; P = 0.0001)
  - cardiovascular death (4.0 vs. 5.1%; HR = 0.79; P = 0.001
  - definite/probable stent thrombosis (2.2 vs. 2.9%; HR = 0.75; P = 0.02)
  - major bleeding (11.6 vs.11.2%; HR = 1.04; P = 0.43),
  - Major bleeding not related to CABG was greater with ticagrelor (4.5 vs. 3.8%; HR = 1.19; P = 0.03).

Wallentin et al. NEJM 2009
Duke ACS Algorithm

Symptoms of Acute Ischemia

Nurse Triage and ECG within 10 minutes
- pain-free, low-mod risk, neg or nonspecific ECG neg. CK-MB, TnT/I

ST↑, LBBB

Enroll in Trials
- non ST↑ ACS, mod-high risk

ASA 325 mg initial dose; 81 mg qD until/at DC

Primary PCI
- Ticagrelor or Prasugrel*
- Bivalirudin or UFH/GP IIb/IIIa

Secondary PCI
- Ticagrelor or Prasugrel
- Bivalirudin or UFH/GP IIb/IIIa

Antithrombotic Rx
- Clopidogrel 600 mg load; 150 mg qD for 7d or until DC (if PCI)

Chest Pain Unit

< 12h Sx
- Dynamic STΔs, pos. cardiac markers

≥ 12h Sx
- Dynamic STΔs, neg. cardiac markers

Anticoagulant Rx
- no cath
- cath in 12h

Cath <24 hrs
- UFH *

Cath ≥24 hrs
- Fondaparinux or enoxaparin

Or bivalirudin**

No or delayed cath

*Prasugrel for primary PCI (if no h/o TIA or stroke); **GP IIb/IIIa at time of PCI or if refractory ischemia; **Consider bivalirudin for cath <12 hours

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Plato Substudy of diabetic patients

- 18,624 patients randomized in the PLATO
- 4,662 (25%) were reported as having DM by the investigators
- Analysis highlights issues of trying to draw conclusions from trial data subsets

PLATO DM vs no DM

Primary endpoint death mi stroke

PLATO – Bleeding risk in DM patients

1 Year Mortality in Patients with Diabetes Following PCI with and without Abciximab

EPIC, EPILOG, and EPISTENT - Meta-Analysis

- Placebo n = 574
- Abciximab n = 888

↓ 2.0%
p = 0.031

Bhatt DL et al. JACC 2000; 35:922-28
Platelet therapies in ACS for DM IIb/IIIa in DM meta analysis

6 trials n=6458 all with low use of P2Y12 inhibitors
26% reduction (6.2 TO 4.8) in mortality vs PLACEBO
70% reduction (4.0 TO 1.2) in mortality for those with PCI

EARLY- ACS – An overall negative trial with increased bleeding risk
2860/ 9406 subject with DM (11.7 vs 13.8) p=NS
High use of P2Y12 inhibitors

Rofi Circulation 2001; Giugliano NEJM 2009
Relationship Between Restenosis and Mortality in Diabetic Patients

- 513 diabetic pts underwent 6 month f/u angio and long-term clinical f/u
- 10-yr survival
  - No restenosis: 24%
  - Non-occlusive: 35%
  - Occlusive: 59%
- Occlusive (but not non-occlusive) restenosis associated with strong, independent risk of 10-year mortality (RR 2.4)

Van Belle E et al. Circulation 001;103:1218-24
Meta-analysis: BMS vs DES in Patients With Diabetes

P < .00001
HR = 0.13 (0.09-0.20)
BMS
N = 611

P < .00001
HR = 0.23 (0.16-0.33)
DES
N = 530

In-stent Restenosis

Population, %

TLR

RESET: TLR at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>EES</th>
<th>SES</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Diabetes</td>
<td>3.5</td>
<td>3.7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.2</td>
<td>6.6</td>
</tr>
<tr>
<td>NIDDM</td>
<td>5.1</td>
<td>4.9</td>
</tr>
<tr>
<td>IDDM</td>
<td>5.4</td>
<td>12.3</td>
</tr>
</tbody>
</table>

P = .85
P = .24
P = .92
P = .03

Pooled SPIRIT/COMPARE: 2-Year ARC
Definite/Probable Stent Thrombosis

Stent Thrombosis, %

- Diabetes
  - EES: 1.6 (N = 1188)
  - PES: 2 (N = 681)
  - P = .50
- No Diabetes
  - EES: 2.4 (N = 3056)
  - PES: 0.3 (N = 1855)
  - P < .0001

P_{interaction} < .0006

RESOLUTE Pooled Patient Level Analysis

R-ZES in Non-DM (n = 3595), NIDDM (n = 1080) and IDDM (n = 455)

Clinically driven TLR, %
- Non-DM: 2.9, NIDDM: 3.1, IDDM: 6.3
- P < .001

Cardiac Death/TV-MI, %
- Non-DM: 3.6, NIDDM: 3.8, IDDM: 6.6
- P = .003

ARC Def/Prob stent thrombosis, %
- Non-DM: 0.7, NIDDM: 0.8, IDDM: 1.5
- P = .02

Cumulative Events, %

P values are adjusted with propensity score quintiles.

Primary Endpoint: Target Vessel Failure (TVF): Composite of Cardiac Death, Target vessel MI or Ischemia-Driven TVR at 1-Year
Primary End Point: Target Vessel Failure Rate at 1 Year

PES HR [95%CI] = 1.64 [1.09-2.47]
P = 0.02 by log-rank test
P_N = 0.08 by P-M test
P_CR = 0.005

Cumulative Incidence (%)

Number at risk

<table>
<thead>
<tr>
<th>Months</th>
<th>PES</th>
<th>EES</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>914</td>
<td>916</td>
</tr>
<tr>
<td>3</td>
<td>841</td>
<td>856</td>
</tr>
<tr>
<td>6</td>
<td>818</td>
<td>846</td>
</tr>
<tr>
<td>9</td>
<td>789</td>
<td>820</td>
</tr>
<tr>
<td>12</td>
<td>713</td>
<td>736</td>
</tr>
</tbody>
</table>

*Events calculated with Kaplan-Meier methods and compared with the use of the log-rank test. Differs slightly from graph which were calculated as categorical variables and compared with use of Chi-Square test.

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Stent Thrombosis Rate at 1 Year

HR [95%CI] = 5.08 [1.74-14.87]
P<0.001 by log-rank test

Cumulative Incidence (%)

2.2%
0.5%

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Months</th>
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</thead>
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<tr>
<td></td>
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<tr>
<td>EES</td>
<td>916</td>
</tr>
</tbody>
</table>

*Events calculated with Kaplan-Meier methods and compared with the use of the log-rank test. Differs slightly from graph which were calculated as categorical variables and compared with use of Chi-Square test.
Tuxedo India Conclusions

In this largest DES vs DES trial in diabetics comparing PES vs EES

Primary End Point

1. PES (Taxus) did not meet the non inferiority criteria when compared to EES (Xience).
2. EES (Xience) on superiority analysis proved superior.
3. This superiority was maintained in insulin requiring patients also

Stent thrombosis and myocardial rates were significantly higher with PES
PCI or CABG?
Do Diabetics Have Increased Mortality After Multivessel Stenting?

<table>
<thead>
<tr>
<th>Study (yrs f/u)</th>
<th>Type of Study</th>
<th>N</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARI (8)</td>
<td>RCT</td>
<td>353</td>
<td>1.87 *</td>
</tr>
<tr>
<td>EAST (8)</td>
<td>RCT</td>
<td>90</td>
<td>1.56</td>
</tr>
<tr>
<td>BARI registry (5)</td>
<td>Obs</td>
<td>339</td>
<td>1.29</td>
</tr>
<tr>
<td>Duke databank (6)</td>
<td>Obs</td>
<td>770</td>
<td>1.27</td>
</tr>
<tr>
<td>Emory databank (5)</td>
<td>Obs</td>
<td>889</td>
<td>1.35 *</td>
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<tr>
<td>NNE (2)</td>
<td>Obs</td>
<td>2766</td>
<td>1.49*</td>
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<tr>
<td>ARTS (3)</td>
<td>RCT</td>
<td>210</td>
<td>1.70</td>
</tr>
<tr>
<td>SOS (1)</td>
<td>RCT</td>
<td>142</td>
<td>&gt;10</td>
</tr>
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</table>

**Summary:** Stents do not appear to have significantly attenuated the mortality advantage of CABG in multivessel CAD.
BARI: Impact of Diabetes on Survival

balloon angioplasty era

5 year survival

BARI Subgroups

• Treated diabetic pts only

• **CABG 81%**

• **PTCA 65%**
CARDia Trial Design

Diabetic patients with multi vessel disease or complex single vessel disease

Suitable for PCI or CABG

Inclusion and exclusion criteria met

CONSENT

Up to date CABG

Optimal PCI stent + abciximab

DES 72% EUHS 28%

Randomisation

www.e-Cardio.gr
CARDia: Main conclusions

- No apparent difference between PCI and CABG at 1 year in:
  - Death
  - Composite of death, MI and stroke

- More repeat revascularization in the PCI group

- PCI may now be considered a reasonable strategy in diabetic patients with multivessel disease

- Longer follow up is needed
SYNTAX Trial

- CABG vs PCI in 3 vessel or LMCA disease
  - 60% patients were 3V CAD
  - 40% LMCA disease
  - Paclitaxel was the DES used

- How the score was calculated
  - Amount of segments involved
  - If a CTO was present and if so what type
  - Bifurcation vs trifurcation lesions
  - Ostial lesions
  - Tortuosity
  - Long segment disease
  - Small vessel disease
Results.

- **Composite primary endpoint was higher in PCI vs CABG (17.8% vs 12.4%)**
  - Death/MI/Repeat revascularization
  - This was driven by revascularization (13.5% vs 5.9%)
  - Death/Stroke/MI were comparable
  - At 3 and 5 year follow up, primary endpoint remained higher in PCI group (driven by revascularization)
Purpose of **FREEDOM**

- To determine if contemporary PCI with DES or CABG techniques, both with currently recommended ancillary medical therapies, is the superior approach to revascularization in patients with diabetes and multivessel CAD.
• Exclusion criteria
  – Prior CABG or valve surgery
  – Left main disease
  – \textit{ST-elevation MI in last 72 hours}
  – Prior PCI in 6 months
• **DES**: sirolimus or paclitaxel eluting. Newer generations could be used if approved for use. **ASA and clopidogrel** for at least 12 months.

• CABG: encouraged arterial revascularization when able

• Medical therapy goals for both groups:
  - LDL <70
  - BP <130/80
  - HgbA1c <7%
SYNTAX SCORE

• **Tool to score complexity of CAD based on anatomy**
• There were 395 participants (20.9%) with a high SYNTAX score (>32), 839 (44.0%) with an intermediate score (22-32), and 662 (35.1%) with a low score (<22).
Results

A Primary Outcome

P = 0.005 by log-rank test
5-Yr event rate: 26.6% vs. 18.7%

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>PCI</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years</td>
<td>953</td>
<td>947</td>
</tr>
<tr>
<td></td>
<td>848</td>
<td>814</td>
</tr>
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<td></td>
<td>788</td>
<td>758</td>
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<td></td>
<td>625</td>
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<td>219</td>
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</tr>
</tbody>
</table>
Results

B. Death

P = 0.049 by log-rank test
5-Yr event rate: 16.3% vs. 10.9%

No. at Risk
PCI   953   897   845   685   466   243
CABG  947   855   806   655   449   238
STROKE

![Graph showing stroke rates over years post-randomization for PCI/DES and CABG.]

- **PCI/DES N 953**: 2.4%
- **CABG N 947**: 5.2%

Logrank P=0.034
REPEAT REVASCULARIZATION

Months post-procedure

Repeat Revascularization, %

PCI/DES

CABG

PCI/DES

CABG

Log rank P<0.0001

13% 5%

PCI/DES

CABG

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Results

- Primary outcome analysis for DES type compared to CABG (898 pts)
  - Sirolimus-eluting (469 pts) at 5 yrs: 6.7% more events than CABG
  - Paclitaxel-eluting (394 pts) at 5 yrs: 6.5% more events than CABG
- No difference in 30 day major bleeding event: P=0.13
- ARF requiring dialysis at 30 days significantly higher in CABG group (P=0.02): 8 pts compared to 1 patient
Discussion - limitations

- **Low-prevalence subgroups**
  - Low statistical power to detect interactions between subgroups

- **Unblinded**
  - Investigators argue that this is less important given objective outcomes and similar medical therapy between groups

- **Generalizability: only 10% of screening population eligible, only half of those randomized**
  - Late Breaking Clinic Trial 2012: PI stated that of the eligible patients who declined randomization, *most requested PCI as reason for not wanting randomization*
  - Equipoise candidates for each procedure often not the case. Likely explains significant number of patients screened but not eligible for randomization
Annual and Cumulative Costs: Years 1-5

Δ costs = $7878

Δ costs = $3641

Year 1 Year 2 Year 3 Year 4 Year 5

CABG Annual Cost PCI Annual Cost CABG Cumulative Cost PCI Cumulative Cost

Cumulative

$60,000 $50,000 $40,000 $30,000 $20,000 $10,000 $0

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"[In diabetic patients with complex disease,] CABG was of significant benefit as compared with PCI."

- Dr Valentin Fuster, PI and senior author

"I think the study is very convincing, and I think the guidelines will likely recognize that. There have been trends showing this before, such as the BARI-2D study with similar information showing that surgery was definitely better than medicine. I think that if you look at the anatomy—and all coronary disease is not the same—the anatomy [of diabetics] is imposing, and I think most of these patients go to surgery anyway. But I think this provides meaningful information to help us with these decisions."

- Dr David Williams

"Faced with a patient who is a candidate for either procedure, I would think long and hard about performing PCI at this point."

- Dr Alice Jacobs
Several studies have compared outcomes for CABG and PCI, but most were done before the availability of stenting (2nd and 3rd generation).

Without the use of novel antiplatelet !!!!
Approaches to Improve Late DES Outcomes

1. Metallic DES with bioabsorbable polymers
2. Metallic DES, polymer-free
3. Bioresorbable vascular scaffold (BVS)
Several studies have compared outcomes for CABG and PCI, but most were done before the availability of stenting, which has revolutionized the latter approach.

1st generation
2nd generation
Biolimus-A9 Eluting Stent

Abluminal Bioabsorbable Polymer

BSC Synergy stent

Bioresorbable Vascular Scaffolds (BVS)

Igaki-Tamai

BVS

REVA

BTI

Biotronik

PLA

PLA (everolimus coated)

Iodinated tyrosine-polycarbonate (with PTX)

PAE-saliclylate (with sirolimus)

3d generation

BioFreedom Stent (Biosensors)

Hypothesis: Polymer-free drug release via porous-eluting stents may reduce late events caused by polymer stent coatings.

Potential advantages:
- Avoid long term late adverse effects that might be attributable to the polymer
- Improved surface integrity since there is no polymer to be sheared or peeled away from the stent struts
- Possible shorter need of dual antplatelet therapy

Drug elution controlled by diffusion physics
CABG in Patients with Diabetes

- CABG advantage depends on use of LIMA
- ↑ rates of procedure related morbidity
  - Renal failure
  - Wound infection
  - Sternal wound failure
  - Increased stroke risk

ARTS trial - 1 year CVA rate
- CABG 6.3%  PCI 1.8%
Angiographic Patency after CABG: experience from CLEVELAND CLINIC DATABASE (565+511 days)

- LIMA
- RIMA
- SVG
- RADIAL

Khot u et al. Circulation 2004
Angiographic Patency after CABG: experience from CLEVELAND CLINIC DATABASE (565+511 days)

- LIMA
- RIMA
- SVG
- RADIAL

> 70%

Khot u et al. Circulation 2004
PCI with 3d generation DES and novel antiplatelet or CABG?

Thank you!!!!