PCI with Drug-Eluting Stents vs. CABG in Left Main Coronary Artery Disease: An Individual Patient Data Meta-Analysis

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Disclosures

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Background

• PCI with drug-eluting stents or CABG may be considered for the treatment of unprotected left main CAD in patients with low to intermediate anatomical complexity\textsuperscript{1,2,3}

• Data comparing these two revascularization strategies stem principally from 4 landmark RCTs: SYNTAX (LM subgp),\textsuperscript{4} PRECOMBAT,\textsuperscript{5} NOBLE,\textsuperscript{6} and EXCEL\textsuperscript{7}

• However, differences in trial composite endpoints and findings have led to persistent uncertainty among clinicians and practice guideline committees regarding the optimal revascularization strategy

CABG, coronary artery bypass grafting; CAD, coronary artery disease; PCI, percutaneous coronary intervention

\textsuperscript{1}EHJ 2019;40:87-165; \textsuperscript{2}Circulation 2014;130:1749-67; \textsuperscript{3}JACC 2017;69:2212-41

Approach

• A collaboration was formed between
  – Independent Investigators: M. Sabatine, B. Bergmark, S. Murphy, P. O'Gara, P. Smith, E. Braunwald
  – Principal Investigators of the four trials: P. Serruys, A. Kappetein, S. Park, D. Park, E. Christiansen, N. Holm, P. Nielsen, G. Stone, J. Sabik

• The Independent Investigators
  – Created the statistical analysis plan
  – Performed all analyses
  – Drafted the manuscript, had complete control over the content, and vouch for the integrity of the analyses and the findings
Methods

• A one-stage meta-analytic approach was used on a combined dataset of individual patient data supplied by each trial

• Primary endpoint: all-cause mortality through 5 years

• 5 Secondary endpoints: cardiovascular death; spontaneous MI; procedural MI; stroke; repeat coronary revascularization

• Landmark analyses; supplemental analyses using 10-year mortality data (available in SYNTAX & PRECOMBAT); subgroup analyses

• Bayesian analyses to help quantify the probability and magnitude of any difference in mortality
# Baseline & Procedural Characteristics

All 4394 patients judged by a Heart Team to be equally suitable candidates for either PCI or CABG

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PCI (N=2197)</th>
<th>CABG (N=2197)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>66 (59-73)</td>
<td>66 (59-72)</td>
</tr>
<tr>
<td>Male</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>SYNTAX score</td>
<td>25 (19-31)</td>
<td>24 (18-31)</td>
</tr>
<tr>
<td>Left main only</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Left main + multivessel (≥2V) disease</td>
<td>52</td>
<td>53</td>
</tr>
<tr>
<td># stents / conduits</td>
<td>2 (1-3)</td>
<td>2 (2-3)</td>
</tr>
<tr>
<td>IVUS use</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>LIMA</td>
<td></td>
<td>96</td>
</tr>
<tr>
<td>All arterial</td>
<td></td>
<td>23</td>
</tr>
</tbody>
</table>

Data presented as median (IQR) or %.
Mortality

HR 1.10 (0.91-1.32)
P=0.33

PCI

CABG

Number at Risk
CABG 2197 2085 2042 2002 1939 1585
PCI 2197 2120 2068 2015 1942 1539

Δ 0.9% (-0.9, 2.8)
Bayesian Analysis of Mortality

86% probability that mortality greater with PCI vs. CABG

49% probability that mortality $\Delta$ between PCI & CABG $\geq 1\%$ over 5 yrs ($\geq 0.2\%/yr$)

5% probability that mortality $\Delta$ between PCI & CABG $\geq 2.5\%$ over 5 yrs ($\geq 0.5\%/yr$)

Absolute risk difference more likely than not $< 0.2\%/yr$
### CV & Non-CV Mortality

<table>
<thead>
<tr>
<th>Type of Death</th>
<th>5-Year KM Rates</th>
<th>∆</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>PCI: 6.2</td>
<td>CABG: 5.9</td>
</tr>
<tr>
<td>Non-CV</td>
<td>5.2</td>
<td>4.5</td>
</tr>
</tbody>
</table>

**CV Mortality**

HR 1.07 (0.83-1.37)

Cumulative Incidence

- Δ 0.4% (<0.1%/yr)
- Δ 0.7%
- Δ 0.3%
- Δ 0.1%
- Δ -0.1%
Two Trials with 10-Year Mortality Data

Cumulative Incidence

HR 0.96 (0.76-1.21)
P=0.72

CABG

PCI

Data from SYNTAX & PRECOMBAT

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>648</td>
<td>657</td>
</tr>
<tr>
<td>0</td>
<td>604</td>
<td>623</td>
</tr>
<tr>
<td>2</td>
<td>577</td>
<td>591</td>
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<tr>
<td>4</td>
<td>531</td>
<td>547</td>
</tr>
<tr>
<td>6</td>
<td>500</td>
<td>519</td>
</tr>
<tr>
<td>8</td>
<td>463</td>
<td>475</td>
</tr>
</tbody>
</table>

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Mortality Analysis Subgroups

- **Age ≥65 years (N=2496)**: HR (95% CI) = 1.23 (0.99-1.51), P_interaction = 0.09
- **Age <65 years (N=1898)**: HR (95% CI) = 0.84 (0.57-1.24)
- **Male (N=3371)**: HR (95% CI) = 1.06 (0.86-1.31), P_interaction = 0.60
- **Female (N=1023)**: HR (95% CI) = 1.18 (0.82-1.71)
- **Diabetes (N=1104)**: HR (95% CI) = 1.11 (0.82-1.52), P_interaction = 0.87
- **No Diabetes (N=3289)**: HR (95% CI) = 1.08 (0.86-1.36)
- **LVEF <50% (N=499)**: HR (95% CI) = 1.01 (0.67-1.53), P_interaction = 0.84
- **LVEF ≥50% (N=3562)**: HR (95% CI) = 1.04 (0.84-1.29)
- **eGFR <60 mL/min/1.73m² (N=531)**: HR (95% CI) = 1.30 (0.89-1.89), P_interaction = 0.23
- **eGFR ≥60 mL/min/1.73m² (N=2568)**: HR (95% CI) = 0.98 (0.75-1.27)

- **SYNTAX score <22 (N=1778)**: HR (95% CI) = 1.06 (0.77-1.48), P_interaction = 0.48
- **SYNTAX score 23-32 (N=1627)**: HR (95% CI) = 0.98 (0.73-1.30)
- **SYNTAX score ≥33 (N=953)**: HR (95% CI) = 1.30 (0.92-1.84)

- **Left main only (N=705)**: HR (95% CI) = 1.39 (0.82-2.36), P_interaction = 0.11
- **Left main + 1 vessel (N=1367)**: HR (95% CI) = 0.79 (0.57-1.11)
- **Left main + 2 vessels (N=1375)**: HR (95% CI) = 1.34 (0.96-1.86)
- **Left main + ≥3 vessels (N=907)**: HR (95% CI) = 1.14 (0.78-1.66)
CV Mortality and SYNTAX Score

\[ P_{\text{interaction}} = 0.15 \]

\[ \text{Hazard ratio for PCI vs. CABG} \]

SYNTAX score

CABG better

PCI better
MI & Repeat Revascularization

Spontaneous MI

HR 2.35 (1.71-3.23); P<0.0001
Absolute Δ 3.5%; NNT$_{5y}$ = 29

Repeat Revascularization

HR 1.78 (1.51-2.10); P<0.0001
Absolute Δ 7.6%; NNT$_{5y}$ = 14
Procedural MI

Protocol Definition

OR 0.65 (0.47-0.92)
P=0.013

PCI: 3.2%
CABG: 4.7%

UDMI (SYNTAX & EXCEL)

OR 1.42 (0.88-2.30)
P=0.15

PCI: 3.2%
CABG: 2.3%

• CK-MB >5× + new Qw [or angio or imaging in some trials]
• [CK-MB >10× in some trials]

• PCI: cTn >5× + ST ∆s, Qw, angio, or imaging [or sx]
• CABG: cTn >10× + Qw, angio, or imaging
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**Stroke**

1st Year
- 13 vs. 35 events
- HR 0.37 (0.19-0.69)
- P=0.002
- Absolute Δ 1.0%

Beyond 1st Year
- 42 vs. 28 events
- HR 1.49 (0.93-2.41)

Cumulative Incidence

Years of Follow-up

HR 0.84 (0.59-1.21)
- P=0.36

CABG
- 3.1%

PCI
- 2.7%
Summary

Comparing PCI w/ DES vs. CABG in Pts w/ LM CAD, median SYNTAX score of 25, and deemed equally suitable candidates for either revascularization approach:

No statistically significant difference in survival at 5 yrs (and 10 yrs)
Bayesian approach suggested $\Delta$ favoring CABG probably exists (more likely than not $<0.2\%/y$)
Possible CV mortality benefit of CABG appeared confined to Pts w/ high SYNTAX scores

Differences in risk of procedural MI depended on the definition used
The nuances of these data emphasize the importance of a Heart Team approach to assist patients in reaching a treatment decision that is best for them.