Lessons learned from EXCEL: what should be taken into account and will the management of myocardial revascularization change in the near future?
Study Design

2900 pts with unprotected left main disease

SYNTAX score ≤32
Consensus agreement of eligibility and equipoise by heart team

No
(N=1000)

Yes
(N=1900)

Enrollment registry

PCI (Xience EES)
(N=950)

CABG
(N=950)

Follow-up: 1 month, 6 months, 1 year, annually through 5 years
Primary endpoint: Measured at a median 3-yr FU, minimum 2-yr FU
Primary Endpoint
All-cause Death, Stroke or MI at 5 Years

Death, stroke or MI (%)

CABG (n=957)
PCI (n=948)

22.0%
19.2%

OR [95% CI] = 1.19 [0.95, 1.50]
P=0.13

Number at risk:
PCI 948
CABG 957

Months

0 12 24 36 48 60

778 783 734 486
809 818 854 818

789 763 738 532

VII ЕЖЕГОДНЫЙ ТРАНСРАДИАЛЬНЫЙ ЭНДОВАСКУЛЯРНЫЙ КУРС / VII TRANSRADIAL COURSE TREC-2020
**Piecewise Hazards**

**All-cause Death, Stroke or MI**

Three distinct periods of varying relative risk

- **CABG (n=957)**
  - 0-day to 30-day HR: 0.61 [95% CI: 0.42, 0.88]; P-value = 0.008
  - 30-day to 1-year HR: 1.07 [95% CI: 0.68, 1.70]; P-value = 0.76
  - 1-year to 5-year HR: 1.61 [95% CI: 1.23, 2.12]; P-value < 0.001

- **PCI (n=948)**
  - 0-day to 30-day HR: 0.61 [95% CI: 0.42, 0.88]; P-value = 0.008
  - 30-day to 1-year HR: 1.07 [95% CI: 0.68, 1.70]; P-value = 0.76
  - 1-year to 5-year HR: 1.61 [95% CI: 1.23, 2.12]; P-value < 0.001

**Treatment-time interaction: P<0.001**

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**Number at risk:**
- PCI: 948, 933, 929, 902, 889, 854, 856, 819, 776, 794, 511, 579
- CABG: 957, 929, 889, 856, 819, 776, 794, 511, 579

**Months**

- 0
- 1
- 12
- 24
- 36
- 48
- 60

**Death, stroke or MI (%)**

- 0-day to 30-day: 4.1% (CABG), 4.9% (PCI)
- 30-day to 1-year: 8.0% (CABG), 4.9% (PCI)
- 1-year to 5-year: 15.1% (CABG), 9.7% (PCI)
Restricted Mean Survival Time Analysis

All-cause Death, Stroke or MI

CABG (n=957)
PCI (n=948)

OR 1.19 [95% CI, 0.95, 1.50]

P=0.13
# Primary Endpoint at 5 Years

All-cause Death, Stroke or MI after Multiple Imputation to Account for Missing Follow-up Data

<table>
<thead>
<tr>
<th>Population</th>
<th>Kaplan-Meier rate (n events)</th>
<th>Odds ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCI</td>
<td>CABG</td>
</tr>
<tr>
<td>All-cause death, stroke or MI</td>
<td>21.8%</td>
<td>19.5%</td>
</tr>
<tr>
<td>- All-cause death</td>
<td>13.0%</td>
<td>10.1%</td>
</tr>
<tr>
<td>- Stroke</td>
<td>3.1%</td>
<td>3.7%</td>
</tr>
<tr>
<td>- Myocardial infarction</td>
<td>10.2%</td>
<td>9.6%</td>
</tr>
</tbody>
</table>

Event rates are binary proportions. Odds ratios and 95% confidence intervals were estimated from time offset logistic regression.
### Adjudicated Causes of Death

<table>
<thead>
<tr>
<th>Category</th>
<th>PCI (N=948)</th>
<th>CABG (N=957)</th>
<th>Difference [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause death</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Definite cardiovascular</td>
<td>13.0% (119)</td>
<td>9.9% (89)</td>
<td>3.1% [0.2%, 6.1%]</td>
</tr>
<tr>
<td>- Sudden cardiac death</td>
<td>5.0% (45)</td>
<td>4.5% (40)</td>
<td>0.5% [-1.4%, 2.5%]</td>
</tr>
<tr>
<td>- Myocardial infarction</td>
<td>1.0% (9)</td>
<td>0.6% (5)</td>
<td>0.4% [-0.4%, 1.2%]</td>
</tr>
<tr>
<td>- Heart failure or cardiogenic shock</td>
<td>0.6% (5)</td>
<td>1.1% (9)</td>
<td>-0.5% [-1.3%, 0.4%]</td>
</tr>
<tr>
<td>- Stroke</td>
<td>1.0% (9)</td>
<td>0.9% (8)</td>
<td>0.1% [-0.8%, 1.0%]</td>
</tr>
<tr>
<td>- Bleeding</td>
<td>0.0% (0)</td>
<td>0.3% (3)</td>
<td>-0.3% [-, -]</td>
</tr>
<tr>
<td>- Other cardiovascular cause</td>
<td>1.0% (8)</td>
<td>0.6% (5)</td>
<td>0.4% [-0.4%, 1.2%]</td>
</tr>
<tr>
<td>- Definite non-cardiovascular</td>
<td>6.6% (58)</td>
<td>4.6% (40)</td>
<td>2.0% [-0.2%, 4.2%]</td>
</tr>
<tr>
<td>- Pulmonary</td>
<td>1.0% (8)</td>
<td>0.6% (5)</td>
<td>0.4% [-0.5%, 1.2%]</td>
</tr>
<tr>
<td>- Infection (includes sepsis)</td>
<td>1.6% (14)</td>
<td>0.8% (7)</td>
<td>0.8% [-0.2%, 1.8%]</td>
</tr>
<tr>
<td>- Gastrointestinal</td>
<td>0.1% (1)</td>
<td>0.2% (2)</td>
<td>-0.1% [-0.5%, 0.3%]</td>
</tr>
<tr>
<td>- Malignancy</td>
<td>3.4% (29)</td>
<td>2.7% (23)</td>
<td>0.7% [-1.0%, 2.3%]</td>
</tr>
<tr>
<td>- Accident/trauma</td>
<td>0.3% (3)</td>
<td>0.2% (2)</td>
<td>0.1% [-0.4%, 0.6%]</td>
</tr>
<tr>
<td>- Non-cardiovascular organ failure</td>
<td>0.2% (2)</td>
<td>0.0% (0)</td>
<td>0.2% [-, -]</td>
</tr>
<tr>
<td>- Other non-cardiovascular cause</td>
<td>0.0% (0)</td>
<td>0.2% (2)</td>
<td>-0.2% [-, -]</td>
</tr>
<tr>
<td>- Undetermined cause</td>
<td>1.9% (16)</td>
<td>1.1% (9)</td>
<td>0.9% [-0.3%, 2.0%]</td>
</tr>
</tbody>
</table>
Limitations

- Blinding of PCI vs. CABG was not possible; some degree of event ascertainment bias cannot be excluded.

- Analyses of secondary endpoints were not adjusted for multiplicity – all hypothesis generating – but all observed differences were relatively modest in magnitude given the 5-year time frame of the present study.

- Under-powered for subgroups; e.g. primary endpoint results were consistent in high SYNTAX score subgroup (25% of pts) - however, further studies are required to determine whether PCI is an acceptable alternative to CABG in LMCAD pts with high anatomic complexity.

- Ten-year follow-up (or longer) is required to characterize the very late safety profile of PCI and CABG as both stents and bypass grafts progressively fail over time.
Conclusions

• In the EXCEL trial, treatment of patients with LMCAD and visually-assessed low or intermediate SYNTAX scores with CoCr-EES resulted in similar rates of the clinically meaningful composite outcome of death, stroke or MI at 5 years.

• The early benefits of PCI due to reduced peri-procedural risk were attenuated by the greater number of events occurring during follow-up with CABG, such that at 5 years the cumulative mean time free from adverse events was similar with both treatments.
Conclusions

• PCI may thus be considered an acceptable revascularization modality for selected patients with LMCAD, a decision which should be made after heart team discussion, taking into account each patient’s individual risk factors and preferences.
Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease


Stone GW et al. NEJM 2019:Sept 28th, on-line
Repeat Revascularization and Mortality After PCI or CABG for LM CAD


**Impact on Mortality of Repeat Revascularization**

- **3-Year All-Cause Mortality**
  - Any repeat revascularization: \( p = 0.02 \)
  - After index PCI: \( P_{int} = 0.85 \)
  - After index CABG:

- **3-Year Cardiovascular Mortality**
  - Any repeat revascularization: \( p < 0.0001 \)
  - After index PCI: \( P_{int} = 0.85 \)
  - After index CABG:

- **PCI** (N = 948)
  - 12.9% underwent repeated revascularization within 3 years
  - 21.1%: Redo-PCI, 79.6%: CABG
  - \( p = 0.0003 \) favoring CABG

- **CABG** (N = 957)
  - 7.6% underwent repeated revascularization within 3 years
  - 9.3%: Redo-CABG, 90.7%: PCI
Repeat Revascularization Within 3 Years After PCI or CABG
<table>
<thead>
<tr>
<th>Class Of Recommendation</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG/PCI</td>
<td></td>
</tr>
<tr>
<td>I—Heart Team approach Recommended</td>
<td>C</td>
</tr>
<tr>
<td>IIa—Calculation of STS and SYNTAX Scores</td>
<td>B</td>
</tr>
<tr>
<td>CABG</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>PCI</td>
<td></td>
</tr>
<tr>
<td>IIa—For SIHD when low risk of PCI complications and high likelihood of good long-term outcome (e.g., SYNTAX score of ≤22, ostial or trunk left main CAD), <strong>and</strong> a significantly increased CABG risk (e.g., STS-predicted risk of operative mortality ≥5%)</td>
<td>B</td>
</tr>
<tr>
<td>IIb—For SIHD when low to intermediate risk of PCI complications and intermediate to high likelihood of good long-term outcome (e.g., SYNTAX score of &lt;33, bifurcation left main CAD) <strong>and</strong> increased CABG risk (e.g., moderate-severe COPD, disability from prior stroke, prior cardiac surgery, STS-predicted operative mortality &gt;2%)</td>
<td>B</td>
</tr>
<tr>
<td>III—Harm—For SIHD in patients (versus performing CABG) with unfavorable anatomy for PCI and who are good candidates for CABG</td>
<td>B</td>
</tr>
</tbody>
</table>
Decision making process

1. A systematic analysis and global appraisal of the patient’s presentation

2. Experience of the centre and operator in patient selection

3. Guidelines based on short-term and long-term results from randomised clinical trials
First PCI of left main in the world

"Third PCI patient ever treated. Forty-three year old man with severe angina pectoris since September, 1977. First angiogram (November 11) revealed severe stenosis of the main L.C.A. . ." (see Fig. 1). (The patient expired suddenly about 4 months after this procedure.)

—Grunzig
Feasibility is not an indication!
Conclusion

Decision should be made after heart team discussion, taking into account each patient’s individual circumstances and preferences.