Long-term Cardiac and Neurocognitive Outcome After Off-pump Coronary Artery Bypass Grafting (OPCAB) Versus Percutaneous Coronary Intervention (PCI) 

The Octopus Study


DISCLOSURES / CONFLICTS OF INTEREST
None reported by all authors.

Participating Centers:
University Medical Center Utrecht
Isala Clinics Zwolle
Antonius Hospital Nieuwegein

Funded by:
Netherlands National Health insurance Council.
Coronary revascularization effectively relieves angina but is associated with adverse effects:

- Brain: stroke, TIA, cognitive decline
- Myocardial damage
- End-organ damage: e.g. renal dysfunction
INTRODUCTION (2)

• CABG with CPB: neuro-cognitive complications. Development of Off-Pump CABG (OPCAB)
  OPCAB: comparable cardiac outcome
  OPCAB: no benefit on cognitive decline

• PCI is equally safe as CABG and OPCAB, but
  Repeat revascularization rate 29% in 5 years
  Procedural stroke 0.5%, TIA 6% and micro-emboli on transcranial doppler
  Cerebral ischemic injury on DWI-MRI
  Cognitive decline comparable to CABG with CPB, but no direct comparison PCI versus OPCAB

1 Van Dijk D et al, *JAMA* 2007
2 Daemen J *Circulation* 2008
4 Lund C *Eur Heart J* 2005
5 Bladin CF, *Stroke* 1998
OBJECTIVES

To compare the long-term effects of PCI versus OPCAB on

[1] Cardiac outcome
DESIGN

• Randomization PCI–BMS *versus* OPCAB

• Long-term follow-up at 7.5 years

• Multi-center

• Patients referred for PCI

• Stable and unstable coronary disease

• Preserved or moderately impaired LV Function

1 van Dijk D, *Controlled Clinical Trials, 2000*
Data collection:
• Physician-confirmed hospital records
• Independent, blinded event committee

Cardiac outcome measure: composite of
• Death
• Myocardial infarction
• Stroke
• Coronary re-intervention
Data collection

• 9 validated neuropsychological tests
• 7 domains of cognition
• Psychologist blinded to randomization

Cognitive outcome measure:

• Overall mean of individual standardized test scores
• Crude analysis
  Multiple imputation (sensitivity for missing values)
FLOW of PATIENTS – 7.5 YEAR FOLLOW-UP

Screened 2263  Eligible 589 (26%)

Randomized 280

PCI  OPCAB
n=138  n=142

CARDIAC OUTCOME
137 included  141 included
1 lost (1%)  1 lost (1%)
99% complete

COGNITIVE OUTCOME
126 alive  122 alive
106 included  106 included
95 included (75%)  87% (87%)
31 lost (25%)  16 lost (13%)
81% complete
## BASELINE CHARACTERISTICS: ORIGINAL SAMPLE

<table>
<thead>
<tr>
<th>BASELINE</th>
<th>PCI  (n=138)</th>
<th>OPCAB (n=142)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years mean (SD)</td>
<td>60 (9)</td>
<td>59 (10)</td>
</tr>
<tr>
<td>Male, %</td>
<td>70</td>
<td>72</td>
</tr>
<tr>
<td>Stroke or TIA, %</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Myocardial infarction, %</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>PCI, %</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>DM, %</td>
<td>9</td>
<td>14</td>
</tr>
<tr>
<td>Coronary disease 1VD, %</td>
<td>68</td>
<td>74</td>
</tr>
<tr>
<td>Normal LVF, %</td>
<td>91</td>
<td>79</td>
</tr>
</tbody>
</table>

## PROCEDURAL

<table>
<thead>
<tr>
<th>PROCEDURAL</th>
<th>PCI</th>
<th>OPCAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stents, n</td>
<td>1.44</td>
<td>0.03</td>
</tr>
<tr>
<td>Arterial grafts, n</td>
<td>0.03</td>
<td>1.1</td>
</tr>
<tr>
<td>Manipulation of aorta, %</td>
<td>100</td>
<td>15</td>
</tr>
</tbody>
</table>
## RESULTS – 7.5 YEAR CARDIAC OUTCOME

<table>
<thead>
<tr>
<th></th>
<th>PCI (n=137)</th>
<th>OPCAB (n=141)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death n(%)</td>
<td>12 (8.7%)</td>
<td>19 (13.4%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.7%)</td>
<td>1 (0.7%)</td>
<td>1.00</td>
</tr>
<tr>
<td>MI</td>
<td>11 (8.0%)</td>
<td>8 (5.6%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Composite Death / Stroke / MI</td>
<td>24 (17.4%)</td>
<td>28 (19.7%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Repeat revascularization</td>
<td>30 (21.7%)</td>
<td>16 (11.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>CABG</td>
<td>4 (2.9%)</td>
<td>1 (0.7%)</td>
<td>0.17</td>
</tr>
<tr>
<td>PCI</td>
<td>26 (18.8%)</td>
<td>15 (10.6%)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>CARDIAC OUTCOME</strong></td>
<td><strong>54 (39.9%)</strong></td>
<td><strong>44 (31.0%)</strong></td>
<td><strong>0.12</strong></td>
</tr>
</tbody>
</table>
## Baseline Characteristics: Cognitive Outcome Sample

<table>
<thead>
<tr>
<th></th>
<th>PCI (n=95)</th>
<th>OPCAB (n=106)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years mean (SD)</td>
<td>59 (8)</td>
<td>57 (9)</td>
<td>0.10</td>
</tr>
<tr>
<td>Education, score</td>
<td>4.1</td>
<td>4.3</td>
<td>0.26</td>
</tr>
<tr>
<td>Male, %</td>
<td>73</td>
<td>73</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke or TIA, %</td>
<td>5</td>
<td>5</td>
<td>0.86</td>
</tr>
<tr>
<td>Myocardial infarction, %</td>
<td>26</td>
<td>23</td>
<td>0.55</td>
</tr>
<tr>
<td>DM, %</td>
<td>9</td>
<td>13</td>
<td>0.41</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>34</td>
<td>32</td>
<td>0.81</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>62</td>
<td>62</td>
<td>0.98</td>
</tr>
<tr>
<td>Coronary disease: 1 VD, %</td>
<td>71</td>
<td>73</td>
<td>0.35</td>
</tr>
<tr>
<td>Normal LVF, %</td>
<td>89</td>
<td>78</td>
<td>0.03</td>
</tr>
</tbody>
</table>
RESULTS – 7.5 YEARS NEUROCOGNITIVE OUTCOME

Cognitive Domains

- Verbal memory
- Motor capacity
- Divided attention
- Reaction time
- Decision making
- Working memory
- Learning

n=201

Mean score

Difference: -0.25 0 0.25 0.5 0.75

PCI BETTER ↔ OPCAB BETTER

P < 0.01
<table>
<thead>
<tr>
<th>OPCAB vs. PCI</th>
<th>Crude</th>
<th>Multiple Imputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect ($\beta$)</td>
<td>0.28</td>
<td>0.25</td>
</tr>
<tr>
<td>95% CI</td>
<td>(0.09-0.47)</td>
<td>(0.08-0.42)</td>
</tr>
<tr>
<td>P-Value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
After 7.5 years, OPCAB was associated with:

- a comparable safety profile as PCI
- a lower risk of coronary re-interventions
- a better cognitive performance.
DISCUSSION

• Cognitive assessment at baseline unavailable. Cognitive outcome is valid only on treatment-group level.

• Mechanism difference in cognitive outcome is unknown. Subclinical cerebral injury may have occurred due to micro-embolization after thoracic aorta manipulation with catheters during (repeated) PCI.

• BMS were used. In DES era, less re-interventions may be expected.
The Octopus Study

• Patients who were treated with OPCAB had better Neurocognitive function compared to the PCI patients after 7.5 years (due to aortic manipulation)

• LIMITATIONS:
  1. Neurocognitive testing was not performed prior to intervention (25% PCI, 13% OPCAB patients not tested)
  2. Lund C, et al Eur Heart J 2005 observed worse neurocognitive function for radial artery compared to femoral techniques and there is no mention of TIA rates
  3. No data on medication effects (e.g. Statins, Aspirin, Warfarin or rates of Atrial Fibrillation)
Transcranial Doppler detection of microemboli during percutaneous transluminal coronary angioplasty.

Bladin CF, Bingham L, Grigg L, Yapanis AG, Gerraty R, Davis SM.

BACKGROUND AND PURPOSE: The use of percutaneous transluminal coronary angioplasty (PTCA) to treat coronary artery disease is now commonplace. The occurrence of microemboli during invasive procedures such as cardiac angiography and bypass surgery is well documented, although neurological complications are relatively uncommon. To date, no investigation has been undertaken of the frequency or nature of microemboli occurring during PTCA or of the correlation with aortic atheroma. METHODS: Twenty patients having elective PTCA underwent examination by transcranial Doppler ultrasonography (TCD) to detect left middle cerebral artery microemboli occurring during the procedure. Blinded off-line analysis correlated microembolic signal counts on TCD with the components of each stage of the PTCA. Patients later underwent transesophageal (TEE) echocardiography, with measurements made of the thickness of the intima and atheroma in the ascending and descending thoracic aortic arch by cardiologists blinded to the TCD results. RESULTS: A total of 973 microembolic signals were detected (mean+/SD, 48.7+/36.7 per patient); 196 (20%) occurred on movement of the PTCA catheter and wire around the aortic arch, 84 (9%) with other PTCA catheter-associated movements, and 679 (70%) in association with injection of solutions (eg, saline and contrast). Mean signal counts during contrast injection were significantly greater than during the other 2 phases (P<0.001). No neurological events occurred in the study. Although not statistically significant, there was a trend toward greater microembolic signal counts with the number of times the catheter was passed around the aortic arch and the amount of arch atheroma detected by transesophageal echocardiography.

CONCLUSIONS: Microemboli detected on TCD are a common occurrence during PTCA but are largely asymptomatic. The majority of microembolic signals are most probably gaseous in origin and do not appear to be related to the extent of aortic atheroma or to clinical events.

The Octopus Study Hypothesis: Subclinical cerebral injury may have occurred due to micro-embolization after thoracic aorta manipulation with catheters during (repeated) PCI.
On-pump versus off-pump coronary-artery bypass surgery.
Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D; Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group.

- BACKGROUND: Coronary-artery bypass grafting (CABG) has traditionally been performed with the use of cardiopulmonary bypass (on-pump CABG). CABG without cardiopulmonary bypass (off-pump CABG) might reduce the number of complications related to the heart-lung machine. METHODS: We randomly assigned 2203 patients scheduled for urgent or elective CABG to either on-pump or off-pump procedures. The primary short-term end point was a composite of death or complications (reoperation, new mechanical support, cardiac arrest, coma, stroke, or renal failure) before discharge or within 30 days after surgery. The primary long-term end point was a composite of death from any cause, a repeat revascularization procedure, or a nonfatal myocardial infarction within 1 year after surgery. Secondary end points included the completeness of revascularization, graft patency at 1 year, neuropsychological outcomes, and the use of major resources. RESULTS: There was no significant difference between off-pump and on-pump CABG in the rate of the 30-day composite outcome (7.0% and 5.6%, respectively; P=0.19). The rate of the 1-year composite outcome was higher for off-pump than for on-pump CABG (9.9% vs. 7.4%, P=0.04). The proportion of patients with fewer grafts completed than originally planned was higher with off-pump CABG than with on-pump CABG (17.8% vs. 11.1%, P<0.001). Follow-up angiograms in 1371 patients who underwent 4093 grafts revealed that the overall rate of graft patency was lower in the off-pump group than in the on-pump group (82.6% vs. 87.8%, P<0.01). There were no treatment-based differences in neuropsychological outcomes or short-term use of major resources. CONCLUSIONS: At 1 year of follow-up, patients in the off-pump group had worse composite outcomes and poorer graft patency than did patients in the on-pump group. No significant differences between the techniques were found in neuropsychological outcomes or use of major resources. (ClinicalTrials.gov number, NCT00032630.). Copyright 2009 Massachusetts Medical Society.