Current Perspective in Off-Pump Coronary Revascularization

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Altoona, PA

CONSULTANT: JOHNSON & JOHNSON
### Morbidity Associated with CPB

- Myocardial Necrosis
- Systemic Inflammatory Response
- Neuro-Cognitive effects / Brain injury
- Pump Lung (Adult Respiratory Distress Syndrome)
- Renal Dysfunction
- Embolization
- Coagulation Disorders
- Increased Blood Loss
- Also cannulation complications and challenges

### OFF-PUMP CABG Challenges

- Technically demanding operation
  - Surgeon
  - Whole the surgical team (off-pump team)
- Requires expertise on the anesthesiologist
- Years of deliberate practice to master this technique / Expert level
- Steep learning curve
Trends in Off-Pump CABG

Off-Pump CABG in 2017: 12.5 %. STS Database
Number of Off-Pump CABGs
20,400 in 2016 (STS database)

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</tr>
</thead>
<tbody>
<tr>
<td>Isolated CABG</td>
<td>164,340</td>
<td>168,027</td>
<td>167,329</td>
<td>160,819</td>
<td>149,652</td>
<td>146,476</td>
<td>147,891</td>
<td>148,214</td>
<td>154,585</td>
<td>156,931</td>
</tr>
<tr>
<td>Isolated Aortic Valve Replacement</td>
<td>18,730</td>
<td>21,376</td>
<td>24,501</td>
<td>25,620</td>
<td>27,255</td>
<td>28,768</td>
<td>30,679</td>
<td>29,840</td>
<td>30,052</td>
<td>28,037</td>
</tr>
<tr>
<td>Isolated Mitral Valve Replacement</td>
<td>4,522</td>
<td>4,845</td>
<td>5,336</td>
<td>5,496</td>
<td>5,676</td>
<td>6,295</td>
<td>6,642</td>
<td>6,989</td>
<td>7,184</td>
<td>7,592</td>
</tr>
<tr>
<td>Aortic Valve Replacement + CABG</td>
<td>15,879</td>
<td>17,536</td>
<td>18,823</td>
<td>18,344</td>
<td>18,214</td>
<td>18,372</td>
<td>18,502</td>
<td>18,384</td>
<td>17,935</td>
<td>17,196</td>
</tr>
<tr>
<td>Mitral Valve Replacement + CABG</td>
<td>2,582</td>
<td>2,576</td>
<td>2,589</td>
<td>2,446</td>
<td>2,322</td>
<td>2,383</td>
<td>2,434</td>
<td>2,641</td>
<td>2,752</td>
<td>2,885</td>
</tr>
<tr>
<td>Aortic + Mitral Valve Replacements</td>
<td>1,285</td>
<td>1,317</td>
<td>1,503</td>
<td>1,468</td>
<td>1,609</td>
<td>1,661</td>
<td>1,777</td>
<td>1,910</td>
<td>1,844</td>
<td>1,964</td>
</tr>
<tr>
<td>Mitral Valve Repair</td>
<td>5,424</td>
<td>6,155</td>
<td>6,817</td>
<td>7,300</td>
<td>7,835</td>
<td>8,394</td>
<td>8,822</td>
<td>8,667</td>
<td>8,943</td>
<td>8,619</td>
</tr>
<tr>
<td>Mitral Valve Repair + CABG</td>
<td>4,854</td>
<td>5,177</td>
<td>4,898</td>
<td>4,759</td>
<td>4,696</td>
<td>4,797</td>
<td>4,293</td>
<td>3,957</td>
<td>3,454</td>
<td></td>
</tr>
</tbody>
</table>

More off-pump CABGs than AVR-CABG, MVR, MVR-CABG, MVP, MVP-CABG and AVR-MVR
• Retrospective studies from specialized centers
• Randomized trials in relatively low risk patients
  • Meta Analysis
• Observational data from large databases
Single Center Studies (by experts)
mostly retrospective reviews

OFF-PUMP CABG IS BETTER

- Lower mortality in high risk groups
- Lower morbidity (all patients)
- Better soft outcomes
- Good quality of revascularization
- Good mid and long-term results:
  - Survival
  - Low rate of re-interventions
Prospective-Randomized Control Trials: Off-Pump Vs. On Pump CABG

Surgeon and Team experience

SMART (Single-197)
> 100 OP
PRAGUE 6 (Single-200)
ON-OFF study (7-401)
250 OP/last 5 years

CORONARY GOPCABE (79-4752)
Median 300 OP
Mean 515 OP

Khan (Single-103)
25 OP year/ 2 years

ROOBY (18-2203)
Median 50 OP CAB, trainees

Expertise in OP CABG by Surgical Team
Prospective-Randomized Control Trials: Off-Pump Vs. On Pump CABG

Surgeon and Team experience

Good

> 100 OP
2 years out
No trainees

Quality of Results

Median 300 OP
Mean 515 OP

COMPARABLE GRAFT PATENCY: OFF-PUMP and ON-PUMP CABG

Graft Patency

Table 2. Early (Inhospital) and Late (1-Year) Arterial and Venous Graft Patency by Coronary Arterial Target

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 372)</th>
<th>Off-Pump</th>
<th>On-Pump</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior descending coronary artery and branches</td>
<td>99/100 (99.0)</td>
<td>99/100 (99.0)</td>
<td>&gt; 0.00</td>
</tr>
<tr>
<td>Right coronary artery and branches (n = 164)</td>
<td>14/14 (100)</td>
<td>12/13 (92.3)</td>
<td>&gt; 0.00</td>
</tr>
<tr>
<td>Uncorrected coronary artery and branches (n = 164)</td>
<td>15/19 (78.9)</td>
<td>15/17 (88.2)</td>
<td>&gt; 0.00</td>
</tr>
<tr>
<td>All coronary arteries (n = 622)</td>
<td>131/131 (100)</td>
<td>129/132 (98.2)</td>
<td>&gt; 0.00</td>
</tr>
</tbody>
</table>

Expertise in OP CABG by Surgical Team

Khan (Single-103)

Low

SMART TRIAL

SMART (Single-197)
30 Day Composite Outcome

Table 3. Primary end point ROOBY

<table>
<thead>
<tr>
<th>End point</th>
<th>ECC (n = 203)</th>
<th>OPCAB (n = 200)</th>
<th>Unadjusted P value</th>
<th>Adjusted P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>27 (13.3)</td>
<td>12 (6.0)</td>
<td>.009</td>
<td><strong>.010</strong></td>
</tr>
<tr>
<td>Operative mortality</td>
<td>7 (3.4)</td>
<td>4 (1.9)</td>
<td>.376</td>
<td>.379</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6 (3.0)</td>
<td>4 (1.9)</td>
<td>.539</td>
<td>.514</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.5)</td>
<td>—</td>
<td>.494</td>
<td>.995</td>
</tr>
<tr>
<td>Renal failure</td>
<td>10 (4.9)</td>
<td>5 (2.4)</td>
<td>.173</td>
<td>.149</td>
</tr>
<tr>
<td>Recipient for bleeding</td>
<td>7 (3.4)</td>
<td>3 (1.4)</td>
<td>.516</td>
<td>.115</td>
</tr>
<tr>
<td>ARDS</td>
<td>—</td>
<td>1 (0.5)</td>
<td>1.000</td>
<td>.995</td>
</tr>
</tbody>
</table>

Note: ROOBY indicates a significant improvement in the adjusted P value for the composite outcome compared to OPCAB.
Prospective-Randomized Control Trials: Off-Pump Vs. On Pump CABG

Surgeon and Practice Experience

5 year MACE

- SMART (Single-197)
- PRAGUE 6 (Single-200)
- ON-OFF study (7-401)

> 100 OP
2 years out
No trainees

Quality of Results

Good

Khan (Single-103)
250 OP
Last 5 years

Low

Expertise in OP CABG by Surgical Team

CORONARY GOPCABE (79-4752)

ROOBY (12-2394)

Figure 1. Kaplan-Meier Curves for the Second Endpoints Outcome at 5 Years.

The second endpoint outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction (receiving or not receiving percutaneous intervention), or reoperation for vascular complications. The inset shows the same data on an expanded x-axis.

No. at Risk
On-pump CABG
Off-pump CABG

Hazard ratio, 95% CI, 1.13 (1.06-1.21)

Probability of freedom from MACE

No. at Risk
On- pump treatment
Off- pump treatment

Hazard ratio for MACE, 1.13 (95% CI, 1.05-1.21)

Years since Study CABG
Prospective-Randomized Control Trials: Off-Pump Vs. On Pump CABG

Early and Modern era

Good

Quality of Results

Poor

Low

Expertise in OP CABG by Surgical Team

High

Modern era

Coronary (79-4752)

Early era

Khan (Single-103)

ROOBY (18-2203)

NEJM 2004

NEJM 2009

NEJM 2012

NEJM 2013

ACC 2013 PRAGUE 6 (Single-200)

JAMA 2004 SMART (Single-197)

JTCVS 2012 ON-OFF study (7-401)
Comparison of Pooled Outcomes for Mixed-Risk and High-Risk Patients

### Outcomes according to Risk

**On-PUMP vs. OFF-PUMP**

- **Lower Mortality and morbidity in high-risk groups**
- **Lower morbidity in all risk groups**

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**Meta Analysis**

- **37 RCT:** 3,300 Pts
- **42 Non RCT:** 26,349 Pts

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**Mixed-Risk Patients [Level A]** = Cheng 2004 (37 randomized trials; 3369 patients)

**Mixed-Risk Patients [Level B]** = Beattie 2004 (13 non-randomized trials; 198,204 patients) or Reston 2003 (53 trials; 46,621 patients)

**High-Risk patients [Level B/A]** = ISMICS Consensus Meta-Analysis 2004 (42 non-randomized trials and 3 randomized trials; 26,349 patients)

Current evidence of coronary artery bypass grafting off-pump versus on-pump: a systematic review with meta-analysis of over 16 900 patients investigated in randomized controlled trials

Ange Christin Deppe; Wasim Arian; Elmar W. Kuhn; Ingo Slootsch; Maximilian Schenker; Oliver J. Lappopoulos; Yeong-Hoon Choi; Thorsten W{"a}hner


**OPCAB reduces risk for**
- *Stroke*
- *Low Cardiac-Output Syndrome*
- *Renal Dysfunction*
- *Infection*
- *Patients receiving Transfusion*

**OPCAB increases risk for**
- *Repeat Revascularization*
**Large Database Studies**

**NY Database** (close to 50,000 Pts.)
- Lower surgical mortality and morbidity
- Higher rate of repeat revascularization
  
  *Hannan et al. Circulation 2007*

**NY Database** (close to 68,000 Pts.)
- Lower surgical morbidity
- Higher mid term mortality *no in the last 2 years*
- Higher mid term rate of repeat revascularization
  
  *Racz et al. JACC 2004*

**STS Database** (close to 15,000 pts)
- Lower surgical mortality in high-risk groups

*Puskas et. Al. Ann Thorac Surg 2009*

**HCA Database** (close to 7,000 Pts-all women)
- Lower surgical mortality and morbidity

*Mack et al. Circulation 2004*

**STS Database** (close to 120,000 Pts)
- Lower surgical mortality and morbidity

*Cleveland et al. Ann of Thorac Surg 2001*

**California Database (CCROP)** (30,000 Pts)
- Lower rate of stroke

*Li et al. Ann Thorac Surg 2010*

**New Jersey Dept. Health Registry** (22,000 Pts)
- Higher repeat revascularization
- Lower 10 year survival

*Chikwe et al. JACC 2018*

- **Green**: Lower Surgical Mortality and Morbidity
- **Yellow**: Higher repeat revascularization
- **Red**: Higher long term mortality
Surgical Mortality
Higher Risk, higher benefit of Off-Pump

STS 2009: Puskas y col.
• Retrospective. STS database
• 14,766 consecutive CABG patients at Emory
• 17 surgeons.
• Analyzed in 4 quartiles stratified by risk, as defined by the STS PROM equation

<table>
<thead>
<tr>
<th>PROM Range</th>
<th>OPCAB Deaths (%)</th>
<th>CAB Deaths (%)</th>
<th>OPCAB Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%-0.75%</td>
<td>5/1824 (0.3)</td>
<td>6/1883 (0.3)</td>
<td>0.86 (0.26, 2.82)</td>
<td>0.80</td>
</tr>
<tr>
<td>0.75%-1.3%</td>
<td>15/1755 (0.9)</td>
<td>17/1921 (0.9)</td>
<td>0.97 (0.48, 1.94)</td>
<td>0.92</td>
</tr>
<tr>
<td>1.3%-2.5%</td>
<td>19/1665 (1.1)</td>
<td>37/2025 (1.8)</td>
<td>0.62 (0.36, 1.08)</td>
<td>0.09</td>
</tr>
<tr>
<td>&gt;2.5%</td>
<td>58/1839 (3.2)</td>
<td>124/1854 (6.7)</td>
<td>0.45 (0.33, 0.63)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Stroke and global neurological adverse events

**Lower in the Off-PUMP population**

<table>
<thead>
<tr>
<th>OFF-PUMP</th>
<th>ON-PUMP</th>
<th>P value</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6%</td>
<td>2%</td>
<td>0.003</td>
<td>Racz et al. 68,000 patients</td>
</tr>
<tr>
<td>1.2%</td>
<td>1.5%</td>
<td>0.0006</td>
<td>Hannan et al. 50,000 patients</td>
</tr>
<tr>
<td>1.25%</td>
<td>1.5%</td>
<td>0.001</td>
<td>Cleveland et al. 118,000 patients</td>
</tr>
<tr>
<td>1.4%</td>
<td>2.1%</td>
<td>0.002</td>
<td>Mack et al. 7,300 patients</td>
</tr>
<tr>
<td></td>
<td>OR 1.8</td>
<td></td>
<td>Marui et al. 3,700 patients (high-risk)</td>
</tr>
<tr>
<td>1.03</td>
<td>1.79</td>
<td>0.006</td>
<td>Mack et al. 7,376 pts (all female)</td>
</tr>
</tbody>
</table>

### Delirium

<table>
<thead>
<tr>
<th>OFF-PUMP</th>
<th>ON-PUMP</th>
<th>P value</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2%</td>
<td>8%</td>
<td>0.001</td>
<td>Bucerlus et al. 16,000 patients</td>
</tr>
</tbody>
</table>
Coronary Artery Bypass Grafting With and Without Manipulation of the Ascending Aorta
A Network Meta-Analysis

Dong Fang Zhao, RA, J. James Edelman, PhD, Michael Seco, MBBS, Paul G. Bannor, PhD
Michael K. Wilson, MBBS, Michael J. Byron, PhD, Vinod Thourani, MD, Andre Lamy, MD, MBBS,
David P. Taggart, PhD, John D. Pusino, MD, Michael P. Valley, PhD

J Am Coll Cardiol 2017;69:924–36

Stroke

- Bayesian network meta-analysis.
- 13 studies / 37,720 patients

<table>
<thead>
<tr>
<th>An Aortic OP CAB (no touch technique)</th>
<th>ON-PUMP CABG</th>
<th>OP CAB</th>
<th>ON-PUMP CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0.4%</strong></td>
<td><strong>1.8%</strong></td>
<td><strong>1.3%</strong></td>
<td><strong>1.8%</strong></td>
</tr>
</tbody>
</table>

78% Relative Risk Reduction

35% Relative Risk Reduction
OFF-PUMP CABG
Quality of revascularization

- Off-PUMP is associated with a higher rate of repeat revascularization
- 0.2 more grafts/patient in the ON-PUMP groups
- Better graft patency in the ON-PUMP groups

- Driven by worse patency in vein grafts
  - Technical (easier to perform LIMA-LAD OFF-PUMP than graft on the non LAD (often veins))
  - Run off
  - Biology (combination of relative hypercoagulable post OFF-PUMP + low endothelial cell viability in SVG)

- Early studies (Rooby, Khan) the difference is more significant
  - Inexperienced OFF-PUMP teams
  - Off-Pump Equipment
  - Vessel loops around the vessels
  - Heparin management
  - Antiplatelet therapy management
• Off-Pump CABG performed by inexperienced surgeons and teams will produce suboptimal results and will be reflected in randomized trials, database studies, meta-analysis and, more importantly, in clinical practice

• If OFF-PUMP CABG performed at an expert level, could obtain (in addition to the short term benefits in mortality and morbidity) the graft patency and long term outcomes of ON-PUMP CABG?
Maturation Process

• **Individual program maturation** – overcoming the learning curve-acquiring expert level

• **Maturation of the Off-Pump techniques-technology. The second decade**
  • Stabilizer
  • Position devices
  • Shunts
  • Misted blower
  • Anastomotic devices
  • Flow evaluation

*Subramanian et al.*
The Failed Promise of OPCAB

There is no heavier burden than a great potential.

Linus
—Charles Schultz
Where OP CAB fits in this era?

Patients who are high risk (for CPB) would benefit the most by OP CAB.

Risk / benefit Ratio

Risk associated with technical adverse events

Benefits in avoiding CPB

Expertise of OP CAB Team critical
Trade offs

On-Pump

Less early morbidity
Reduced long-term graft patency?
Increased repeat revascularization
Long-term survival?

Off-Pump

Myocardial ischemic injury,
Neurocognitive deficits,
Stroke
Inflammatory pathways
Pulmonary, renal, and hematologic complications

Lower mortality in The high-risk groups

Sousa Uva 2017
Cardiac Surgeons and OP CAB

- Surgeons who have never done OP CAB
- Surgeons who have done OP CAB but they don’t do it any more
  - Performed some OP CAB and abandon it
  - Perform OP CAB routinely and then abandon it
- Surgeons who consistently perform OP CAB in their practice

Other reasons:
- Poor results
- Out of comfort zone
- Peer or Institutional pressure
- Response to emerging data
OP CAB
Institutional perspective

• High-risk cases who would benefit the most from OP CAB

• Complement Minimally Invasive Programs
  
  • MID CAB or MICS
  • Robotic Assisted MID CAB
  • TE CAB

• Isolated
• Hybrid Revascularization:
  • LIMA-LAD + Stenting to Non-LAD vessels
Final Remarks

• OP CAB will continue a refinement and maturation process
  • GOALS:
    • Continue the process to decrease the risk of mortality and morbidity (Safer operation)
    • Improve on areas such as graft patency/complete revascularization
    • Perioperative Anticoagulation/antiplatelet management/conduit selection
    • Patient selection (risk/benefit ratio)

• Should be strongly considered for high-risk patients

• Excellent technique to complement innovative approaches

• Should be performed by experienced teams with a systematic approach
THANK YOU