Hybrid Coronary Revascularization: is it prime time?

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Case Presentation (1)

• Mr. TF, 78 yo, male, presented with two month H/O progressive exertional chest pain, radiated to left arm. He denies SOB, DOE, palpitation, or syncope.
• Stress nuclear study showed TID and mild anterior wall reversible defect. Stress EKG developed diffuse ST depression in anterior and lateral leads 3 min into stress test.
• PMH: HTN, DM, Hypothyroidism, remote H/O colon Ca
Case Presentation (2)

- Cath showed:
  - 90% stenosis in proximal LAD
  - 90% stenosis in proximal LCX leads to two large OMs
  - 70% proximal RCA and 90% mid PDA
  - SYNTAX Score: 27
  - EF 55%. Wall motion is normal
  - LVEDP 16 mmHg

Kaplan-Meier curves of cumulative rates according to type of bypass graft

CABG: Long Term Graft Patency

Long Term Patency of SVG by Vessels (VA Cooperation Study)

Can We Improve Revascularization Outcomes Beyond CABG and PCI: Hybrid Revascularization
CABG versus PCI in DES Era

BARI, SIRIUS, TAXUS, ENDEVOR, SPIRIT, & PREVENT IV Trials

Hybrid Coronary Revascularization

Standardizing definitions for hybrid coronary revascularization

Ralf E. Harskamp, MD,1,5* Johannes O. Bonatti, MD,2 David X. Zhao, MD, PhD,3 John D. Puskas, MD,4 Robbert J. de Winter, MD, PhD,5 John H. Alexander, MD, MHS,6 and Michael E. Haikos, MD7

The Journal of Thoracic and Cardiovascular Surgery - February 2014

<table>
<thead>
<tr>
<th>Guideline/registry</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011 ACCF/AHA/GSIC: GUIDELINES FOR PCI, 2011 ACCF/AHA GUIDELINES FOR CABG</td>
<td>The planned combination of LITA-LAD artery grafting and PCI of ≥1 non-LAD coronary arteries. Hybrid coronary revascularization may be performed in a hybrid suite in a single operating setting or as a staged procedure (PCI and CABG) performed in 2 different operating suites, separated by hours to 1 day, but typically during the same hospital stay. Planned, intentional combination of CABG, with a catheter-based intervention in other coronary arteries during the same hospitalization. Procedures can be performed consecutively or in a hybrid operating room or sequentially in the conventional surgical and PCI environments.</td>
</tr>
<tr>
<td>2010 ESC/SCM Guidelines on Myocardial Revascularization</td>
<td>A hybrid procedure is defined as a procedure that combines surgical and transcatheter intervention approaches: (1) planned, concomitant in the same setting; (2) planned, staged, if performed in the same hospital admission; (3) unplanned in performance after unsuccessful revascularization or graft closure during the same hospitalization.</td>
</tr>
<tr>
<td>STS Adult Cardiac Registry National Database (version 2.73)</td>
<td>Minimal invasive LITA-to-LAD and PCI of non-LAD lesions. Procedure can be performed either in the same operating room or during the same hospitalization.</td>
</tr>
</tbody>
</table>
Definition of HCR

Hybrid Coronary Revascularization:
Planned combination of surgical and percutaneous techniques in two different coronary territories, both scheduled and performed within a predefined time period in a patient with multi-vessel coronary artery disease

Hybrid CV Procedures
Multiple Potential Achilles’ Heels

- **Bleeding**
  - P2Y12 inhibitors
- **Stent thrombosis**
  - Protamine reversal
- **Catheter related complication**
  - Retroperitoneal hematomas, strokes, etc
- **Infectious complications**
  - Multiple moving parts and more traffic
- **Renal complications**
  - Nephrotoxic contrast
- **Added time and cost**
  - Is it worth it?
Current Data on HCR

Since 1996 multiple single centers’ experience for a total of >3000 patients treated with HCR. CABG was performed before PCI in one half of HCR procedures, PCI was performed first in 26% and one stop/combined procedure was the least popular choice (22.8%).


Single vs Two Stage of HCR

JACC 2015;65:85-9
### CABG versus “One Stage” Hybrid Post-Op Clinical Outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>CABG N=254</th>
<th>Hybrid N=112</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Stroke</td>
<td>3 (1.1%)</td>
<td>2 (1.7%)</td>
<td>0.48</td>
</tr>
<tr>
<td>New atrial fibrillation</td>
<td>61 (24%)</td>
<td>22 (19%)</td>
<td>0.21</td>
</tr>
<tr>
<td>New intra-aortic balloon pump</td>
<td>7 (3%)</td>
<td>6 (5%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Intra-stent thrombosis</td>
<td>N/A</td>
<td>1 (1%)</td>
<td>N/A</td>
</tr>
<tr>
<td>New low cardiac output syndrome</td>
<td>5 (1.9%)</td>
<td>5 (4.5%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Deep sternal wound infection</td>
<td>3 (1%)</td>
<td>2 (1.8%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Operative mortality</td>
<td>4 (1.5%)</td>
<td>3 (2.6%)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Zhao et al, JACC 2009;53:232-24

### CABG versus “One Stage” Hybrid Post-Op Renal Function

<table>
<thead>
<tr>
<th>Variables</th>
<th>CABG N=254</th>
<th>Hybrid N=112</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Creatinine @ 24 hours (mg/dL)</td>
<td>0.9 (0.3-12.1)</td>
<td>0.9 (0.4-5)</td>
<td>0.90</td>
</tr>
<tr>
<td>Median Creatinine @ 48 hours (mg/dL)</td>
<td>1 (0.4-12.3)</td>
<td>1 (0.3-5.9)</td>
<td>0.78</td>
</tr>
<tr>
<td>Median Creatinine @ 72 hours (mg/dL)</td>
<td>1 (0.3-13.2)</td>
<td>1 (0.4-4)</td>
<td>0.58</td>
</tr>
<tr>
<td>New acute renal failure*</td>
<td>10 (3.9%)</td>
<td>3 (2.6%)</td>
<td>0.39</td>
</tr>
<tr>
<td>25% increase in creatinine@72 hours</td>
<td>89 (35%)</td>
<td>37 (33%)</td>
<td>0.40</td>
</tr>
<tr>
<td>New renal failure requiring hemodialysis</td>
<td>3 (1%)</td>
<td>0 (0%)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Zhao et al, JACC 2009;53:232-24
CABG versus “One Stage” Hybrid Post-Op Bleeding Complication

<table>
<thead>
<tr>
<th>Variables</th>
<th>CABG N=254</th>
<th>Hybrid N=112</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median chest tube drainage (L)</td>
<td>1.3±1.8</td>
<td>1.5±2.1</td>
<td>0.18</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>7 (3%)</td>
<td>3 (3%)</td>
<td>0.63</td>
</tr>
<tr>
<td>Median PRBC transfusions (units) @ 48h</td>
<td>1 (0-20)</td>
<td>1 (0-10)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

- ASA 81mg
- Plavix 300mg loading before induction
- Heparin 70U/Kg with ACT ~250 for PCI (PCI before CABG in 96% cases)
- Additional Heparin to reach ACT 400 when CABG starts
- Protamine to reverse ACT to ~150

Zhao et al, JACC 2009;53:232-241

30 Days MACE by Euro Score
Death/MI/CVA/LCOS

<table>
<thead>
<tr>
<th>Euro Score</th>
<th>Low Euro Score</th>
<th>High Euro Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CABG (8/162)</td>
<td>Hybrid (3/60)</td>
</tr>
<tr>
<td></td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>(8/162)</td>
<td>(3/60)</td>
</tr>
<tr>
<td></td>
<td>12%</td>
<td>15%</td>
</tr>
<tr>
<td></td>
<td>(10/85)</td>
<td>(8/51)</td>
</tr>
</tbody>
</table>

Zhao et al, J Thoracic & Card Surg 20

p=NS
30 Days MACE by SYNTAX Score
Death/MI/CVA/LCOS


30 Days MACE by Euro/Syntax Scores
Death/MI/CVA/LCOS

Hybrid Cardiac Intervention Improves Clinical Outcomes in High Risk Patients

High risk Valve/CABG + PCI

Predicted Mortality*  Observed Mortality

* STS algorithm for preop risk assessment for valve/CABG at time of PCI

Consecutive HCR vs. CABG vs. PCI Propensity Matched/Single Center

Liuzhong Shen et al. JACC 2013;61:2525-2533
Consecutive HCR vs. CABG vs. PCI Propensity Matched/Single Center

HCR vs OPCAB in Patients with DM
HCR vs CABG: Comparative Effectiveness

HCR versus CABG 30 days: Meta-Analysis

Table 3. Thirty-Day Major Adverse Cardiopulmonary and Cardiac Events and In-Hospital Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HCR (n = 309)</th>
<th>CABG (n = 918)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite of 30-d death, MI, stroke, a (%)</td>
<td>10 (3.2)</td>
<td>24 (3.1)</td>
<td>1.07 (0.52-2.21)</td>
<td>0.85</td>
</tr>
<tr>
<td>Death</td>
<td>5 (1.6)</td>
<td>10 (1.1)</td>
<td>1.50 (0.53-4.49)</td>
<td>0.46</td>
</tr>
<tr>
<td>MI</td>
<td>2 (0.7)</td>
<td>8 (0.9)</td>
<td>0.75 (0.36-1.59)</td>
<td>0.22</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 (1.0)</td>
<td>16 (1.7)</td>
<td>0.56 (0.26-1.14)</td>
<td>0.16</td>
</tr>
<tr>
<td>In-hospital major morbidity, a (%)</td>
<td>26 (8.4)</td>
<td>142 (15.5)</td>
<td>0.55 (0.36-0.83)</td>
<td>0.005</td>
</tr>
<tr>
<td>Renal failure</td>
<td>11 (3.6)</td>
<td>51 (5.6)</td>
<td>0.77 (0.47-1.28)</td>
<td>0.32</td>
</tr>
<tr>
<td>Prolonged ventilation &gt;24 h</td>
<td>16 (5.1)</td>
<td>102 (11.1)</td>
<td>0.46 (0.28-0.78)</td>
<td>0.006</td>
</tr>
<tr>
<td>Acute site infection</td>
<td>9 (3.0)</td>
<td>11 (1.2)</td>
<td>——</td>
<td>——</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reading outcome</th>
<th>HCR (n = 309)</th>
<th>CABG (n = 918)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG-related bleeding, a (%)</td>
<td>22 (7.2)</td>
<td>83 (9.1)</td>
<td>0.78 (0.49-1.24)</td>
<td>0.29</td>
</tr>
<tr>
<td>Need for blood transfusion, a (%)</td>
<td>66 (21.5)</td>
<td>611 (66.6)</td>
<td>0.51 (0.30-0.87)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event parameters</th>
<th>HCR (n = 309)</th>
<th>CABG (n = 918)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short PONS, &lt; 1</td>
<td>163 (52.4)</td>
<td>379 (41.8)</td>
<td>1.38 (1.15-1.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>Long PONS &gt; 14 d</td>
<td>7 (2.3)</td>
<td>40 (4.3)</td>
<td>0.40 (0.21-0.78)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Given regression results were used: HCR, hybrid coronary revascularization; OR, odds ratio; PONS, postoperative length of stay.

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J Cardiothorac Surg 2015;10:1
HCR versus CABG at One-year of Follow-up: Meta-Analysis

HCR vs CABG for Multivessel CAD RCT
NIH Hybrid Observational Study

• Prospective cohort observational study
• 11 US sites
• To inform design of an RCT of HCR vs. multi-vessel PCI

JACC 2016;68:356
NIH Hybrid Observational Study

NIH Hybrid Coronary Revascularization RCT

Rationale for Hybrid Revascularization

- The LIMA to the LAD graft has a 20-year patency rate as high as 90%; LIMA to LAD has been associated with reduced angina and revascularization compared to PCI in pts with isolated proximal LAD ds., and a survival benefit compared to PCI in pts with multivessel ds.
  - Caveat – no studies with contemporary DES
- For non-LAD vessels, the SVG is the still most common graft, despite a high failure rate
  - Pan-arterial revascularization is rare, even by excellent operators in non-complex ds. (eg 24.8% in EXCEL)
- Contemporary DES are believed to have substantially improved long-term event-free survival than SVGs (no RCTs)
NIH Hybrid Coronary Revascularization RCT

Randomized Trial of Hybrid Coronary Revascularization vs. PCI

2,354 pts at up to 100 sites with MVD involving the LAD distribution eligible for both HCR and PCI with DES

HCR with LIMA to LAD + PCI with DES of non-LAD vessels

Multivessel PCI with DES of all vessels, including the LAD

Follow-up: 30 days, 1 year and annually through 5 years

Primary endpoint:
- 5-year MACCE (death, MI, stroke, repeat revascularization)
- Powered to detect superiority of HCR over PCI

NIH Hybrid Coronary Revascularization RCT

Randomized Trial of Hybrid Coronary Revascularization vs. PCI

Endpoints

• Primary endpoint:
  - 5-year rate of MACCE (death, MI, stroke, or unplanned repeat revascularization)

• Secondary endpoints
  - MACCE at earlier time points, and individual components of MACCE at all time points
  - CCSC angina score
  - QoL (SF-12, EuroQoL)
  - Costs and cost-effectiveness
**NIH Hybrid Coronary Revascularization RCT**

**Major inclusion criteria**

- Coronary anatomy requiring revascularization with:
  - MV CAD involving the LAD and/or
  - Distal LM and/or
  - Ostial or mid-shaft LM and disease in at least 1 other epicardial coronary artery and/or
  - LAD disease and involvement of a major diagonal artery, both of which require revascularization

**NIH Hybrid Coronary Revascularization RCT**

**Randomized Trial of Hybrid Coronary Revascularization vs. PCI**

**HCR procedures (at operator discretion)**

- Minimally invasive LMIA-LAD surgery may be performed before, during or after PCI
  - Must be off-pump (without planned cardiopulmonary support), either sternal sparing or non-sternal sparing
  - Mid-CAB (limited anterior or lateral thoracotomy)
  - Robotic Mid-CAB or TECAB (totally endoscopic) is allowed at experienced sites
  - Anastomotic patency should be confirmed with intra-operative transit time Doppler flow prior to closure
HCR: Conclusion

• Equipoise is present as to how to best revascularize patients with multivessel disease involving the LAD
• HCR combines the best attributes of minimally invasive surgery with a LIMA-LAD + PCI with DES to non-LAD vessels, thereby eliminating use of SVGs
• Whether HCR improves long-term event-free survival in appropriate patients and is a cost-effective approach compared to multivessel PCI with DES is unknown
• The large-scale, randomized NHLBI-sponsored HYBRID trial will examine the effectiveness of HCR in pts with multivessel disease involving the LAD: Enrollment starting in 2017!

Ideal Hybrid Revascularization RCT

Multivessel CAD

Hybrid: LIMA+DES  CABG: LIMA+SVG  PCI: DES

Uncoupling LIMA from SVG!

Patency and restenosis/thrombosis
Clinical MACE
Surgery versus Catheter: The Times, They Are a Changin’

- CABG carries excellent long term outcomes but invasive. Benefits appear to be limited to mammary graft
- Stent technologies have advanced substantially.
  - The 10X changes.
  - The disruptive technologies.
  - More to come.

Heart Team
The Power of Alignment

- A culture and business model where
  - Cardiology
  - Cardiac Surgery
  - Cardiac Anesthesia
  - Cardiac Imaging
  - Hospital Administration
- Work as a team
  - Requires financial, programmatic, strategic, geographic ALIGNMENT