Clinical Considerations for CTO Revascularization

*Whom to treat, Who derives benefit and What can we achieve?*

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Patient Selection and Clinical Benefit in CTO Revascularization

Relevant Disclosure

Employment: Chief Medical Officer, Cordis Cardiology/ Johnson & Johnson
CTOs in Perspective

Despite novel technologies/DES, frequency of attempted CTOs has not changed over the past decade

- Technical/procedural challenges
- Misperceptions regarding viability, collateral flow
- Uncertainty regarding which patients may benefit balanced by
- Concern for complications in patients who may not derive clinical benefit

Srinivas et al. *Circulation* 2002
Christofferson et al. *Am J Cardiol* 2005
Kandzari, Angioplasty Summit
Impact of Incomplete Coronary Revascularization
New York State Database for PCI

- 68.9% of MVD patients undergoing PCI had incomplete revascularization
- 30.1% had CTOs and/or ≥2 diseased major vessels with incomplete revascularization
  - Mortality highest in this subgroup (HR 1.36, 1.12-1.66)

Hannan et al. Circulation 2006
Theoretical Rationale for CTO Revascularization
‘Open Artery Hypothesis’

• Increase long-term survival
• Improve left ventricular function
• Electrical stability of myocardium and reduced predisposition to arrhythmic events
• Increased tolerance of future coronary occlusion events
Why the Occluded Artery Trial (OAT) Does Not Apply to CTO Revascularization

- OAT: Subacute (3-28 days) total occlusions following MI
- OAT: Relatively asymptomatic population excluding severe ischemia by functional study, rest angina and multivessel disease
- Absence of improvement in LV function in OAT substudy
  - Baseline LVEF 48% (difficult to improve upon relatively normal)
  - Spontaneous recanalization (TIMI 2/3) observed at 1 year in 25% of medical therapy cohort
  - Reocclusion in ~9% of PCI cohort; no DES
  - Greatest predictor of improved LVEF was having a patent target vessel at 1 year follow up

Hochman et al. NEJM 2006
Dzavik et al. Circulation 2006
Kandzari.AngioplastySummit
## Long-term Survival with Successful CTO Revascularization

Support for the Late Open Artery Hypothesis

<table>
<thead>
<tr>
<th>Trial</th>
<th>Success (N)</th>
<th>Failure (N)</th>
<th>Follow-up Duration (years)</th>
<th>Mortality (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Success</strong></td>
<td>1118</td>
<td>340</td>
<td>6</td>
<td>10.0</td>
<td>19.0</td>
</tr>
<tr>
<td><strong>Failure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOAST-GISE</strong></td>
<td>1491</td>
<td>514</td>
<td>10</td>
<td>26.0</td>
<td>35.0</td>
</tr>
<tr>
<td><strong>Aziz et al.</strong></td>
<td>286</td>
<td>83</td>
<td>1</td>
<td>1.1</td>
<td>3.6</td>
</tr>
<tr>
<td><strong>Hoye et al.</strong></td>
<td>377</td>
<td>166</td>
<td>2.4</td>
<td>2.5</td>
<td>7.3</td>
</tr>
<tr>
<td><strong>British Columbia Cardiac Registry</strong></td>
<td>568</td>
<td>306</td>
<td>5</td>
<td>6.5</td>
<td>12.0</td>
</tr>
</tbody>
</table>

1Ramanathan. TCT2003; 2Suero. JACC 2001; 3Olivari. JACC 2003; 4Aziz. TCT2005; 5Hoye Eur Heart J 2005
Long-term Outcome after Intended Recanalization of Non-acute Coronary Occlusions

### Multivariate Mortality Model

<table>
<thead>
<tr>
<th>Failure</th>
<th>Hazard Ratio</th>
<th>95% Confidence</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per decade)</td>
<td>1.33</td>
<td>1.12 – 1.58</td>
<td>0.001</td>
</tr>
<tr>
<td>EF &lt;50</td>
<td>2.33</td>
<td>1.58 – 3.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivessel CAD</td>
<td>1.62</td>
<td>1.09 – 2.40</td>
<td>0.02</td>
</tr>
<tr>
<td>Prior CHF</td>
<td>1.73</td>
<td>1.10 – 2.76</td>
<td>0.02</td>
</tr>
<tr>
<td>ESRD</td>
<td>2.77</td>
<td>1.36 – 5.66</td>
<td>0.005</td>
</tr>
<tr>
<td>CVD</td>
<td>1.92</td>
<td>1.04 – 3.55</td>
<td>0.04</td>
</tr>
<tr>
<td>COPD</td>
<td>1.64</td>
<td>1.01 – 2.67</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.50</td>
<td>0.99 – 2.27</td>
<td>0.055</td>
</tr>
</tbody>
</table>

Ramanathan and Buller *TCT2003*
Influence of CTO Revascularization on Long-term Outcomes

In-Hospital Outcomes

<table>
<thead>
<tr>
<th></th>
<th>CTO Success n=1491</th>
<th>CTO Failure n=514</th>
<th>P value</th>
<th>Non-CTO n=2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (%)</td>
<td>1.0</td>
<td>2.3</td>
<td>0.02</td>
<td>0.8</td>
</tr>
<tr>
<td>Q MI (%)</td>
<td>0.4</td>
<td>0.8</td>
<td>NS</td>
<td>0.8</td>
</tr>
<tr>
<td>non-Q MI (%)</td>
<td>1.5</td>
<td>3.1</td>
<td>0.02</td>
<td>2.4</td>
</tr>
<tr>
<td>urg re-PCI (%)</td>
<td>1.9</td>
<td>0.2</td>
<td>0.01</td>
<td>2.0</td>
</tr>
<tr>
<td>MACE (%)</td>
<td>3.2</td>
<td>5.4</td>
<td>0.02</td>
<td>3.7</td>
</tr>
</tbody>
</table>

Suero et al. JACC 2001
Clinical Considerations

- Is this patient symptomatic, and how? Angina? Heart failure? Arrhythmia?
- Will successful recanalization improve this patient’s symptoms?
- Will successful recanalization improve this patient’s prognosis?
- What are the risks of attempted recanalization in this patient?
## Predictors of Successful CTO Revascularization

<table>
<thead>
<tr>
<th>Procedural Success</th>
<th>Procedural Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional occlusion</td>
<td>Total occlusion</td>
</tr>
<tr>
<td>Occlusion age &lt; 12 weeks</td>
<td>Occlusion age &gt; 12 weeks</td>
</tr>
<tr>
<td>Length &lt; 15 mm</td>
<td>Length &gt; 15 mm</td>
</tr>
<tr>
<td>Tapered stump</td>
<td>Abrupt cut-off</td>
</tr>
<tr>
<td>No sidebranch at occlusion</td>
<td>Sidebranch present</td>
</tr>
<tr>
<td>No bridging collaterals</td>
<td>Extensive bridging collaterals</td>
</tr>
</tbody>
</table>
## ACROSS Pilot

*Predictors of Procedural Outcome, n=103*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Failed</th>
<th>Successful</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple wires*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1 wire</td>
<td>36% vs. 5%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;2 wires</td>
<td>53% vs. 12%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fluoro time, min</td>
<td>28 vs. 21</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>TIMI 0</td>
<td>24% vs. 7%</td>
<td></td>
<td>0.054</td>
</tr>
<tr>
<td>Support catheter</td>
<td>29% vs. 14%</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Collaterals</td>
<td>23% vs. 10%</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>Female</td>
<td>29% vs. 16%</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Length &gt;15mm</td>
<td>19% vs. 10%</td>
<td></td>
<td>0.24</td>
</tr>
<tr>
<td>Ref &lt;3mm</td>
<td>29% vs. 17%</td>
<td></td>
<td>0.23</td>
</tr>
<tr>
<td>Multivessel dz</td>
<td>23% vs. 15%</td>
<td></td>
<td>0.30</td>
</tr>
</tbody>
</table>

*\( p<0.05 \) in multivariable analysis*

Kandzari, Menown et al. TCT2003
Advances in Procedural Technique

Parallel Wires

Retrograde Wire

Courtesy, Dr. Tsuchikane, Toyohashi Heart Center
**CTO Strategies**

*Principles of Technique*

- ✓ Contralateral angiography
- ✓ Multiple views
- ✓ Guiding catheter selection

- ✓ Wire/device selection
- ✓ Incremental stiffness ('drilling') vs. ‘penetration’
- ✓ Parallel/Seesaw wiring, STAR
- ✓ IVUS
- ✓ Retrograde via collaterals

↑ Success vs. Complications
MDCT CTA for Complex Lesion Morphologies

‘CT Facilitated PCI’
Myocardial Viability, Collateral Flow, and Regional Wall Motion

Cardiac MR Imaging

44 pts, 58 CTO segments

Collateral flow did not predict:
1. Myocardial viability
2. Regional improvement following revascularization

Kim, Shah, Kandzari et al AHA 2003

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## Cardiac MR Imaging in CTO Revascularization

*Influence of Revascularization on Wall Motion and LVEF*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
<th>%Δ</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LVEF, %</strong></td>
<td>43.2 ± 8.1</td>
<td>47.6 ± 7.1</td>
<td>4.4 ± 6.1</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>WMS</strong></td>
<td>1.10 ± 0.79</td>
<td>0.52 ± 0.76</td>
<td>-0.59 ± 0.63</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values expressed as mean ± SD

Median follow up 139 days; N=20
Cardiac MR Imaging in CTO Revascularization

Influence of Revascularization on Wall Motion and LVEF

Change in Ejection Fraction Following PCI

% Viable, Dysfunctional Segments in CTO Region

R=0.717
P=0.0012
MR Imaging of Myocardial Viability and Performance in CTO Revascularization

- <50% infarction
- LV dysfunction
CTO Revascularization: Myocardial Performance
MR Imaging to Identify Revascularization Candidates

1 year post PCI
Normal wall motion
Recovery of LV Function After CTO Recanalization

Most Improvement with Baseline LV Dysfunction

- Normal LV Function
  - N=52
- Regional LV Dysfunction
  - N=19
- Global LV Dysfunction
  - N=48

\( p < 0.001 \)

\( p = \text{NS} \)

\( p < 0.001 \)

Werner et al. Am Heart J 2005
Kandzari.AngioplastySummit
Recovery of LV Function After CTO Recanalization

Predictors of Improvement in LV Function

Positive
- Baseline LV dysfunction
- Preserved microvasculature

No Effect
- Collateral development
- Prior MI
- Duration of occlusion
- Nonocclusive restenosis

Negative
- Reocclusion

Werner GS, Am Heart J, 2005
Kandzari.AngioplastySummit
PRISON II

% Outcome

In-stent ABR

In-segment ABR

TLR

MACE

P<0.0001

36

P<0.001

41

P=0.001

19

P<0.001

20

Bx Velocity

Cypher SES

P<0.001

7

11

4

4

P<0.001

19

4

20

P=0.001

11

4

4

<0.001

7

19

MACE
7 month angiographic follow-up: 92 mm DES
Late Incomplete Apposition and Aneurysm Formation

Late Stent Malapposition by IVUS: 25.7% of CTOs
Hong et al. Circulation 2006
Persistence

*If at first you don’t succeed*
Practical Considerations
Developing a CTO Program

• Attend CTO meetings and workshops
• Start with ‘less complex’ coronary CTOs or peripheral (eg, SFA) CTOs
• Perform CTOs with a partner
• Choose a dedicated CTO day
• Be versatile and willing to change strategy
• Be patient and willing to accept failure
Patient Selection and Clinical Benefit in CTO Revascularization

Summary

• The ‘Last Great Barrier to PCI Success’— most frequently encountered yet least treated lesion subset

• Major advances in CTO treatment are: technique/strategy, wire technology, noninvasive imaging for patient selection

• Despite advances, there is no systematic evidence that procedural outcomes have changed for the better or worse
  • *New techniques and therapies introduce new complications*
  • *Need CTO-specific clinical trials that better inform procedural and late outcomes*

• Pathophysiologic rationale to support late open artery hypothesis
  • *Consistency in late survival with CTO revascularization*
  • *LV dysfunction and viability are greatest predictors of improvement*