Chronic Total Occlusions

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Hippocrates Hospital
CTO/ Definitions

• The presence of TIMI 0 flow within the occluded segment with an estimated occlusion duration of > 3 months

• Encountered in 15-30% of patients undergoing cor. Angio

• >50% are symptomatic
Chronic Total Occlusion (CTO)
From Randomized Trials to Daily Practice

<table>
<thead>
<tr>
<th>Trial, Years (Ref. #)</th>
<th>Patients, n</th>
<th>Design</th>
<th>CTO in Trial</th>
<th>Impact of CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASS, 1974-1979 (28)</td>
<td>3,372</td>
<td>Registry of nonrandomized surgical cohort</td>
<td>NA</td>
<td>(\text{Mortality in patients with either severe angina or ejection fraction &lt; 35}%)</td>
</tr>
<tr>
<td>MASS-II, 1995-2000 (30,31)</td>
<td>611</td>
<td>Randomization to CABG, PCI, or medical therapy</td>
<td>NA</td>
<td>(\text{PCI arm: CR in 41}%). (\text{Cardiovascular mortality in CR. Survival 90.6}%) in CR vs. 84.4% IR ((p = 0.04))</td>
</tr>
<tr>
<td>BARI, 1988-1991 (32)</td>
<td>1,829</td>
<td>Randomization to PCI or CABG</td>
<td>60% excluded due to PCI unsuitability of 8,000 screened</td>
<td>No differences</td>
</tr>
<tr>
<td>ERACI II, 1996-1998 (34)</td>
<td>450</td>
<td>Randomization to PCI or CABG</td>
<td>CTO not attempted in CTOs (23.4%)</td>
<td>No data on CR. (\text{MACE in CABG (Freedom from MACE 76.4}%) in CABG vs. 65.3% in PCI, (p = 0.013))</td>
</tr>
<tr>
<td>SoS, 1996-1999 (35)</td>
<td>988</td>
<td>Randomization to PCI or CABG</td>
<td>CTOs excluded from trial</td>
<td>No data on CR. (\text{Mortality in CABG compared with PCI (6.8}%) vs.10.9%)</td>
</tr>
<tr>
<td>SYNTAX, 2005-2007 (37,39,40)</td>
<td>1,800</td>
<td>3-vessel disease or left main disease; randomization to PCI or CABG</td>
<td>23%</td>
<td>(\text{CR in high and intermediate syntax scores. CR with CABG. Cardiac mortality with high syntax score at 1 yr and intermediate at 3 yrs})</td>
</tr>
<tr>
<td>New York State PCI Reporting System, 1997-2000 (43)</td>
<td>21,945</td>
<td>PCI registry</td>
<td>NA</td>
<td>(\text{Mortality (adjusted hazard ratio: 1.35) in IR patients compared with CR in the presence of either a single IR CTO or = 2 IR vessels})</td>
</tr>
</tbody>
</table>

*J Am Coll Cardiol. 2014;63(12_S). S0735-1097(14)61634-X*
CTO Surgical revascularization/ SYNTAX trial

Overall 68.1% of TO were successfully bypassed

Reason not bypassed:
- Not intended to treat (n=12)
- Diseased (n=11)
- Inadequate conduit (n=2)
- Too small (n=19)
- Unable to find (n=1)
- Other (n=36)
SYNTAX trial
Incomplete revascularization predicts adverse outcomes

Farooq V et al, Circulation. 2013
Complete vs Incomplete Revascularization

Table 2. Adjusted HR (IR and IR Subgroups vs. CR) and 95% CI for 18-Month Mortality and Mortality/MI by Subgroups of IR

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>No. of Cases</th>
<th>Mean Length of Follow-up (Months)</th>
<th>No. of Events</th>
<th>Adjusted HR* (95% CI)</th>
<th>p Value</th>
<th>No. of Events</th>
<th>Adjusted HR† (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>3,499</td>
<td>19.0</td>
<td>165</td>
<td>Reference</td>
<td></td>
<td>216</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>IR</td>
<td>7,795</td>
<td>18.9</td>
<td>551</td>
<td>1.23 (1.04–1.45)</td>
<td>0.01</td>
<td>736</td>
<td>1.27 (1.09–1.47)</td>
<td>0.002</td>
</tr>
<tr>
<td>Subgroups of IR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 IR vessel with no total occlusion</td>
<td>3,815</td>
<td>18.9</td>
<td>239</td>
<td>1.23 (1.02–1.48)</td>
<td>0.03</td>
<td>316</td>
<td>1.22 (1.04–1.44)</td>
<td>0.02</td>
</tr>
<tr>
<td>1 IR vessel with total occlusion</td>
<td>1,725</td>
<td>19.1</td>
<td>112</td>
<td>1.11 (0.87–1.42)</td>
<td>0.39</td>
<td>145</td>
<td>1.14 (0.92–1.41)</td>
<td>0.24</td>
</tr>
<tr>
<td>≥2 IR vessels with no total occlusion</td>
<td>1,233</td>
<td>19.1</td>
<td>92</td>
<td>1.18 (0.89–1.56)</td>
<td>0.26</td>
<td>132</td>
<td>1.34 (1.04–1.73)</td>
<td>0.03</td>
</tr>
<tr>
<td>≥2 IR vessels with total occlusion</td>
<td>1,022</td>
<td>18.4</td>
<td>108</td>
<td>1.44 (1.14–1.82)</td>
<td>0.002</td>
<td>143</td>
<td>1.50 (1.21–1.86)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

J Am Coll Cardiol Intv 2009;2:17–25
Complete vs Incomplete Revascularization

U.K. Central Cardiac Audit Database for all CTO PCI compare outcomes of patients with successful versus unsuccessful PCI to a CTO
N=13,443

Success rate 70.6%

Complexicity

Clinical Justification
Angina

Dyspnea

Ischemia

Prognosis
Symptoms in CTO

• Angina (less prominent)
• Dyspnea
• Fatigue
• Patients minimize symptoms
• Often inappropriately labeled asymptomatic

EuroIntervention 2014;9:1165-1172
FACTOR Trial

SAQ Angina Frequency
9.5 (1.6, 17.5)

SAQ Physical Limitation
13.1 (5.1, 21.1)

SAQ Quality of Life
20.3 (11.9, 28.6)

Effect of Procedural Success

*Circ Cardiovasc Qual Outcomes. 2010;3:284-290*
FACTOR Trial

Asymptomatic
- SAQ Angina Frequency: 4.3 (-5.4, 13.9)
- SAQ Physical Limitation: 6.3 (-5.0, 17.6)
- SAQ Quality of Life: 8.5 (-3.7, 20.7)

Symptomatic
- SAQ Angina Frequency: 10.3 (-0.8, 21.3)
- SAQ Physical Limitation: 15.9 (5.1, 26.7)
- SAQ Quality of Life: 27.3 (16.5, 38.0)

Effect of Procedural Success


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ERCTO Registry
Significant Improvement of Angina and Dyspnea

Galassi et al, JACC. 2015
Ischemia

- N=1697

![Pie chart showing distribution of EF (Ejection Fraction): EF >55% (51%), EF 35-55% (32%), EF <35% (17%).]

The Canadian Multicenter Chronic Total Occlusions Registry

Collateral flow in CTO

European Heart Journal (2006) 27, 2406–2412
Coronary Collaterals

**Rentrop Classification**

Grades of collateral filling from the contralateral vessel

<table>
<thead>
<tr>
<th>CLINICAL STUDIES</th>
</tr>
</thead>
</table>

Changes in Collateral Channel Filling Immediately After Controlled Coronary Artery Occlusion by an Angioplasty Balloon in Human Subjects

K. Peter Rentrop, MD, FACC, Marc Cohen, MD, FACC, Heiner Blanke, MD, Robert A. Phillips, MD, PhD
New York, New York

0 : none
1 : filling of side branches of the artery to be dilated via collateral channels without visualization of the epicardial segment
2 : partial filling of the epicardial segment via collateral channels;
3 : complete filling of the epicardial segment of the artery being dilated via collateral channels.

- Experimental data: 90% stenosis of a epicardial coronary artery
- Provides adequate LV contractility
- Provides adequate metabolic needs in hibernating myocardium

Specific pts
Specific cnd
Prevalence of Ischaemia in CTO

$[^{15}O]H_2O$ PET

- Collateral function during increased blood flow demand in viable myocardium is predominantly insufficient.

- Even in the presence of angiographically well-developed collateral arteries, the vast majority of CTO patients with a preserved LVEF showed significantly impaired perfusion.

Stuijfzand et al. EHJ Cardiovasc Imaging. 2016
Ischemia LVEF improved 3 years after PCI@CTO

MRI N = 21
Before, 5m, 3yrs
2 viability indexes used
transmural extent of infarction (TEI)
and end-diastolic wall thickness

Am J Cardiol 2008;101:179–185
Catheterization and Cardiovascular Interventions 2014;83:9–16
FFR was similar in patients with poorly developed (CC 0), intermediate (CC 1), and well developed (CC 2) collaterals
Ischemia FFR@CTO

![Graph showing FFR distribution for different segments of the heart: Akinetic, Hypokineti, Normal.](image)

Catheterization and Cardiovascular Interventions 2014;83:9–16
Prognostic Impact of CTO
SCAAR (Swedish Registry)

HR: 1.41 95%CI: 1.35-1.48
p-value: <0.001

Cumulative Mortality (%) vs Time in years

<table>
<thead>
<tr>
<th>Time in years</th>
<th>Number at Risk CTO</th>
<th>Number at Risk non CTO</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>14,269</td>
<td>74,373</td>
</tr>
<tr>
<td>1</td>
<td>11,009</td>
<td>58,408</td>
</tr>
<tr>
<td>2</td>
<td>9,015</td>
<td>47,639</td>
</tr>
<tr>
<td>3</td>
<td>7,163</td>
<td>37,365</td>
</tr>
<tr>
<td>4</td>
<td>5,447</td>
<td>28,218</td>
</tr>
<tr>
<td>5</td>
<td>3,797</td>
<td>19,270</td>
</tr>
<tr>
<td>6</td>
<td>1,773</td>
<td>9,204</td>
</tr>
</tbody>
</table>

DECISION-CTO

Optimal Medical Therapy With or Without Stenting For Coronary Chronic Total Occlusion

Seung-Jung Park, MD., PhD.

Heart Institute, University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea
Study Flow

834 patients randomized from 2010.3.22 to 2016.10.10

19 withdrew consents

398 allocated to OMT

310 treated with OMT
72 treated with PCI
5 treated with OMT after failed PCI
11 had incomplete data

417 allocated to PCI

346 treated with PCI (success rate: 90.6%)
29 treated with OMT
36 treated with OMT after failed PCI
6 had incomplete data

1-year FU
348/357 (97.5%)

3-year FU
215/231 (93.1%)

5-year FU
87/99 (87.9%)

1-year FU
344/354 (97.2%)

3-year FU
218/238 (91.6%)

5-year FU
85/102 (83.3%)
Primary End Point
(Death, MI, Stroke, Any Repeat Revascularization)

ITT Population

Crude HR 0.95 (95% CI, 0.74-1.22), P=0.67
Adjusted HR 0.91 (95% CI, 0.68-1.23), P=0.54

<table>
<thead>
<tr>
<th>Years Since Randomization</th>
<th>OMT</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>398</td>
<td>417</td>
</tr>
<tr>
<td>1</td>
<td>305</td>
<td>293</td>
</tr>
<tr>
<td>2</td>
<td>246</td>
<td>241</td>
</tr>
<tr>
<td>3</td>
<td>178</td>
<td>175</td>
</tr>
<tr>
<td>4</td>
<td>129</td>
<td>117</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>65</td>
</tr>
</tbody>
</table>

No. at Risk

Probability (%)
Death from any cause

Crude HR 1.50 (95% CI, 0.75-3.03), P=0.25

ITC Population

No. at Risk

<table>
<thead>
<tr>
<th>Year</th>
<th>OMT</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>1</td>
<td>344</td>
<td>337</td>
</tr>
<tr>
<td>2</td>
<td>285</td>
<td>285</td>
</tr>
<tr>
<td>3</td>
<td>207</td>
<td>202</td>
</tr>
<tr>
<td>4</td>
<td>140</td>
<td>142</td>
</tr>
<tr>
<td>5</td>
<td>81</td>
<td>74</td>
</tr>
</tbody>
</table>
Death from any cause

<table>
<thead>
<tr>
<th></th>
<th>OMT</th>
<th>PCI</th>
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<tbody>
<tr>
<td>ITT Population</td>
<td></td>
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<tr>
<td>No. at Risk</td>
<td></td>
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<td>417</td>
</tr>
<tr>
<td>PCI</td>
<td>344</td>
<td>337</td>
</tr>
<tr>
<td>1 Year</td>
<td>285</td>
<td>285</td>
</tr>
<tr>
<td>2 Years</td>
<td>207</td>
<td>202</td>
</tr>
<tr>
<td>3 Years</td>
<td>140</td>
<td>142</td>
</tr>
<tr>
<td>4 Years</td>
<td>81</td>
<td>74</td>
</tr>
</tbody>
</table>

Cardiac Death:
- OMT: 3.6%
- PCI: 1.9%
- P = 0.22

Non-CD:
- OMT: 1.6%
- PCI: 1.2%
- P = 0.31
Myocardial Infarction

Crude HR 0.77 (95% CI, 0.49-1.19), P=0.24

<table>
<thead>
<tr>
<th>Years since Randomization</th>
<th>OMT No. at Risk</th>
<th>PCI No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>398</td>
<td>417</td>
</tr>
<tr>
<td>1</td>
<td>317</td>
<td>300</td>
</tr>
<tr>
<td>2</td>
<td>260</td>
<td>255</td>
</tr>
<tr>
<td>3</td>
<td>189</td>
<td>181</td>
</tr>
<tr>
<td>4</td>
<td>129</td>
<td>125</td>
</tr>
<tr>
<td>5</td>
<td>73</td>
<td>64</td>
</tr>
</tbody>
</table>

ITT Population
Myocardial Infarction

ITT Population

![Graph showing the probability of myocardial infarction over time for periprocedural and spontaneous events. The graph compares the OMT and PCI groups, with P-values of 0.35 and 0.93, respectively.]

<table>
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<tr>
<th>Years since Randomization</th>
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<tr>
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<tr>
<td>1</td>
<td></td>
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<tr>
<td>2</td>
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<td></td>
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<tr>
<td>3</td>
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<tr>
<td>4</td>
<td></td>
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<tr>
<td>5</td>
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</tr>
</tbody>
</table>

- Periprocedural events:
  - OMT: 7.8%
  - PCI: 9.7%
  - P = 0.35

- Spontaneous events:
  - OMT: 1.8%
  - PCI: 1.8%
  - P = 0.93

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>At Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>OMT</td>
<td>398</td>
</tr>
<tr>
<td>PCI</td>
<td>417</td>
</tr>
</tbody>
</table>

CardioVascular Research Foundation
Stroke

Crude HR 2.56 (95% CI, 0.80-8.17), P=0.11

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>OMT</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
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<td>337</td>
</tr>
<tr>
<td>2</td>
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<td>284</td>
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<td>3</td>
<td>203</td>
<td>201</td>
</tr>
<tr>
<td>4</td>
<td>137</td>
<td>142</td>
</tr>
<tr>
<td>5</td>
<td>77</td>
<td>74</td>
</tr>
</tbody>
</table>

No. at Risk
Repeat Revascularization

Crude HR 0.81 (95% CI, 0.52-1.28), P=0.38

No. at Risk
OMT
PCI
398
417
330
321
270
259
292
181
292
129
129
74
65

Years since Randomization

Probability (%)
Repeat Revascularization

ITT Population

No. at Risk
OMT | 398 | 330 | 270 | 292 | 129 | 74
PCI | 417 | 321 | 259 | 181 | 129 | 65

Years since Randomization

Probability (%)

OMT
PCI

CTO lesion

P=0.93

6.2
7.3

P=0.33

4.7
6.1

Non-CTO lesion

10.4%
8.6%

14.0%
11.8%
EUROCTO TRIAL

Study flow chart

Multivessel CAD including CTO

Treat non-occlusive disease by PCI before CTO with DES

29%

Angina or angina-equivalent symptoms

Single-vessel disease CTO only

48%

Randomisation 2:1

PCI with DES + OMT
n=259

OMT
n=137

PCI with DES

Success

Failure

Decision as per usual clinical care

Medical Rx

CABG

Clinically indicated interim PCI

Ongoing angina despite OMT
n=10 (7.3%)

Repeat Exercise Tolerance Test (ETT) for objective assessment of ischemia @ 12m and 36 months

Efficacy: Health status @ 12 months
Safety: Death, non-fatal myocardial infarction (ITT, PP) @ 36 months

OMT to include:
- Aspirin,
- Statin,
- ACE-inhibitor where tolerated
  - + at least 2 anti-anginal agents at max tolerated dose including rate-limiting agent where appropriate. Ischaemic symptoms should be confirmed with non-invasive test.
Primary endpoint: SAQ health status (ITT)

For multiple testing the significance level is 0.01
Changes in CCS class during follow-up

P<0.001

OMT
Baseline | Follow-up
---|---
CCS 1 | CCS 2 | CCS 3 | CCS 4

PCI
Baseline | Follow-up
---|---
CCS 1 | CCS 2 | CCS 3 | CCS 4

EURO CTO trial investigators
Patient affected by CTO

Presence of symptoms

Yes

Normal wall motion or hypokinesia in CTO territory

No

Akinesia or dykinesia in CTO territory

Viability demonstration

Yes

CTO revascularization is indicated

No

Medical therapy is indicated

Ischemic burden evaluation

<10%

≥10%

CTO revascularization is indicated

Galassi et al. EHJ 2016
4 OPTIONS TO CROSSING CTOs

- Antegrade Wire Escalation (AWE)
- Antegrade Dissection Re-entry (ADR)
- Retrograde Dissection Re-entry (RDR)
- Retrograde Wire Escalation (RWE)

TCT 2015
Επεμβατική Καρδιολογία

Κ. Τούτουζας
Η. Ελευθεριάδης
Γ. Λάτσιος
Α. Μαυρογιάννη
Γ. Σιάνος
Ε. Σκαλίδης
Α. Συνετές

Πρόλογος
Χ. Στεφανάδης
Ι. Καλλικάζαρος