Predictors of success in CTO PCI

DR. KHALED SHOKRY
PROFESSOR OF CARDIOLOGY
MILITARY MEDICAL ACADEMY

Chronic total occlusion (CTO) of a coronary artery is defined as an obstruction of a native coronary artery with no visible luminal continuity for at least 3 months.

CTO occurs in approximately one-fourth (15% to 23%) of patients who undergo conventional coronary angiography (CCA).

CTO revascularization remains challenging, with success rates range between 60% to 80%.

(JACC: VOL.8, NO.7, 2015)
Location of CTO

- Proximal RCA: 30.4%
- Distal RCA: 16.0%
- Obtuse Marginal: 12.8%
- Distal LAD: 8.6%
- Proximal LAD: 8.4%
- Distal Cx: 8.4%
- Proximal Cx: 7.4%
- LADD: 5.0%
- PDA/PLV/AMARG: 3.0%

50% of coronary CTO occurs in RCA

Christofferson et al AJC 2005;95:1088

Histopathology of the CTOs

- Most CTOs are not completely occluded when examined under the microscope. They are characterized by a mix of luminal plaque, thrombin, fibrin, inflammatory cells (in the intima, media and adventitia), and neovascular channels.

- The proximal and distal caps have higher concentration of collagen inside the plaque and calcium (fibrocalcific) while the composition of the core correlates with CTO age.
Published indications for CTO revascularization largely mirror the indications for revascularization in otherwise similar non occlusive stable CAD.

In this regard, the primary indication for CTO PCI in the setting of single-vessel CAD is the relief of ischemic symptoms that persist despite anti ischemic medical therapy.

Neither American nor European guidelines distinguish between CTOs and non occlusive lesions with respect to the threshold for undertaking revascularization, whether by PCI or CABG.

The European guidelines consider CTO PCI a complex procedure that demands experienced operators at centers with specialized CTO equipment and access to circulatory support and cardiac surgery. Ad hoc treatment is discouraged.
The American College of Cardiology (ACC) guidelines state that “(CTO PCI) in patients with appropriate clinical indications and suitable anatomy is reasonable when performed by operators with appropriate expertise” (class IIa, level of evidence B) but do not further define appropriateness.

### CTO case selection

- So, the decision to attempt PCI for coronary CTO requires an individualized risk / benefit analysis includes:

  - **Clinical factors**
    - Potential benefits
  - **Angiographic factors**
    - Potential risks
Clinical factors

- Patient’s age.
- Symptom severity.
- Associated comorbidities (eg. DM, chronic renal insufficiency).
- Overall functional status.
- Patient suitability to take dual antiplatelet therapy.
- Waiting for non-cardiac surgery.
- Patient’s tolerance for long procedure.
- Objective evidence of viability in the territory of the occluded artery.

Angiographic factors

- Coronary CTO is the lesion subtype in which angioplasty is most likely to fail.
- So, predicting the difficulty of CTO crossing with a guidewire is important for case selection and procedural planning.
The Japanese chronic total occlusion (J-CTO) score identified five independent predictors of procedural success:

1. Calcification,
2. Bending >45° in the CTO segment,
3. Blunt proximal cap,
4. The length of the occluded segment >20 mm, and
5. Previously failed attempt.
This scoring model was developed by applying 1 point for each of these independent variables when present.

The CTO case complexity was stratified into:
- **Easy** (J-CTO score = 0),
- **Intermediate** (a score = 1),
- **Difficult** (a score = 2), and
- **Very difficult** (a score = 3 - 5)

The J-CTO score correlated well with the probability of successful guidewire crossing within 30 minutes (87.7%, 67.1%, 42.4%, and 10.0%, respectively) and was recently validated in an independent single-center Canadian cohort.

Although, J-CTO score is a useful tool for predicting successful guidewire crossing of the CTO within 30 min., but it failed to predict final procedural success rate.
More recent, a new scoring model, taking into consideration both Clinical and Angiographic parameters and able to predict final CTO – PCI success was published.

<table>
<thead>
<tr>
<th>TABLE 5</th>
<th>Independent Predictive Variables Scored</th>
<th>OR</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe calcified lesion</td>
<td>2.72</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>Previous CABG</td>
<td>2.49</td>
<td>+1.5</td>
<td></td>
</tr>
<tr>
<td>Lesion length ≥20 mm</td>
<td>2.04</td>
<td>+1.5</td>
<td></td>
</tr>
<tr>
<td>Previous MI</td>
<td>1.60</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>Blunt stump</td>
<td>1.39</td>
<td>+1</td>
<td></td>
</tr>
<tr>
<td>Non-LAD CTO location</td>
<td>1.56</td>
<td>+1</td>
<td></td>
</tr>
</tbody>
</table>

OR = odds ratio; other abbreviations as in Table 1.

- These are the independent predictors of unsuccessful CTO – PCI scored according to the corresponding OR size.
Four subgroups were identified on the basis of the success rate:

* Class 0 = Score of 0 – 1 ...... High probability of CTO-PCI success.
* Class 1 = Score of >1 – <3 ... Intermediate probability of CTO-PCI success.
* Class 2 = Score of ≥ 3 – <5 ... Low probability of CTO-PCI success.
* Class 3 = Score of ≥ 5 .......... very Low probability of CTO-PCI success.

According to this score, the probability of failure increased significantly from class to class i.e from 15.1% to 25.1% to 41.1% to 68.1% respectively.

Recent reports showed that the J-CTO score predicts an increasing need for using a hybrid-based CTO algorithm to increase the rate of success.
The “hybrid Strategy” for CTO PCI is a method to standardize initial and provisional technique selection based on patient anatomy.

Antegrade, retrograde, and dissection & reentry techniques are complementary and necessary for the full spectrum of CTO PCI.

Sequential CTO crossing options can increase success, shorten procedure times, and reduce radiation exposure.

The CTO expert operator needs flexibility to accommodate the wide range of anatomic scenarios for chronic occlusion that will be present in patients with strong indications for revascularization.

Five main reasons for attempting to open a CTO:

1. Potential mortality benefit after successful revascularization
2. Relief of angina
3. Improvement in ischemic burden in asymptomatic patients or those with minimal symptoms
4. Improvement in LV function
5. Improved tolerance for future ischemic events
The earliest study that demonstrated mortality benefit was by Suero and colleagues published in 2001. This remains the single largest observational series, with more than 2000 patients followed for more than 10 years, which provides great insights regarding CTO PCI.

In this study, there was a distinct 10-year survival advantage for successful CTO treatment compared with failed CTO treatment (73.5% vs. 65.1%, p < 0.001). The CTO versus non-CTO 10-year survival was the same (71.2% vs. 71.4%, p = 0.9).
This is another small study. Four hundred nineteen consecutive patients scheduled for PCI of CTO. At one-year follow-up, patients with successful PCI of a CTO had a significantly better clinical outcome than those whose PCI was unsuccessful.

In the Mayo Clinic experience of 1262 patients, Prasad and colleagues demonstrated that successful PCI of a CTO conferred a mortality benefit when compared with an unsuccessful attempt. This mortality benefit did not manifest until 6 years, there was a 4% relative risk reduction in mortality per year after 6 years in the group with successful CTO recanalization versus the group with unsuccessful recanalization.
However the evidence from all these studies came from comparing the outcomes in successful and failed CTO procedures without a control group.

This trial was a prospective, multicenter (19) open-label randomized trial comparing **optimal medical therapy with or without stenting** for coronary CTO patients with silent ischemia, stable angina, or ACS. The goal of this trial was to assess the safety and efficacy of CTO-PCI compared with OMT among patients with at least one CTO.
Study goals:

- This trial designed to compare the effects of PCI vs OMT on the 12-month health status of patients with a CTO.

- During longer term follow-up, the study will also assess the safety at 3 years of PCI as compared to OMT for a CTO in stable coronary artery disease.

- It is conducted in 26 European centers from 2012–2015 and organized by the CTO club.

- At 12 months, patients who underwent CTO PCI had less angina, less physical limitation.
2) Relief of angina

<table>
<thead>
<tr>
<th>Study</th>
<th>FU months</th>
<th>No. with successful PCI</th>
<th>No. with symptom relief at FU (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holmes et al JACC 1984</td>
<td>7</td>
<td>13</td>
<td>10 (77)</td>
</tr>
<tr>
<td>Keriakes et al JACC 1985</td>
<td>7</td>
<td>40</td>
<td>30 (75)</td>
</tr>
<tr>
<td>Serruys et al EHJ 1985</td>
<td>7</td>
<td>28</td>
<td>18 (64)</td>
</tr>
<tr>
<td>DiSciascio et al AHJ 1986</td>
<td>8</td>
<td>29</td>
<td>16 (55)</td>
</tr>
<tr>
<td>Melchior et al AJC 1987</td>
<td>8</td>
<td>49</td>
<td>40 (82)</td>
</tr>
<tr>
<td>Finci et al AJC 1990</td>
<td>24</td>
<td>100</td>
<td>57 (57)</td>
</tr>
<tr>
<td>Warren et al AHJ 1990</td>
<td>31</td>
<td>20</td>
<td>16 (80)</td>
</tr>
<tr>
<td>Bell et al Circulation 1992</td>
<td>32</td>
<td>234</td>
<td>178 (76)</td>
</tr>
<tr>
<td>Ruocco et al AJC 1992</td>
<td>24</td>
<td>160</td>
<td>110 (69)</td>
</tr>
<tr>
<td>Ivanhoe et al Circulation 1992</td>
<td>48</td>
<td>286</td>
<td>106 (69)</td>
</tr>
<tr>
<td>Stewart et al JACC 1993</td>
<td>14</td>
<td>45</td>
<td>36 (69)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1004</td>
<td>702 (70%)</td>
</tr>
</tbody>
</table>

Despite the aforementioned studies in which angina relief was substantially higher in patients with successful CTO recanalization versus those in which CTO revascularization was unsuccessful, there remains a large amount of skepticism because the studies were in the balloon angioplasty or bare metal stent era when restenosis and reocclusion were both high and the success rates were 60% to 65%.

Two contemporary trials have attempted to systematically look at this subject.
The first was a single-center prospective cohort analysis performed in the UK. Patients with successful revascularization had less physical activity limitation, rarer angina episodes, and greater patient satisfaction compared with patients with a failed procedure (P<.03 for all 3 components) with improved overall acceptable quality level scores.

The second contemporary trial that systematically evaluated QOL with the SAQ was the FlowCardia Approach to CTO Recanalization (FACTOR) trial. The benefit of successful PCI was greatest in patients who were symptomatic at baseline compared with asymptomatic patients.
Frequently, on diagnostic angiograms, large collaterals are noted to supply the territory of the CTO. This is often mentioned as a rationale for managing patients conservatively and deferring an intervention on CTO. This is a misconception based on the view that the collateral circulation is preventing the development of ischemia in the territory of the CTO.

In this study direct assessment of collateral function by measuring pressure and flow velocity in the collateralized epicardial segment distal to the occlusion. Results showed that collateral circulation is insufficient to prevent ischemia. So, it concluded that even ‘well-collateralized’ CTOs may benefit from a revascularization.

Many trials showed the improvement in LV systolic function after CTO recanalization especially in patients without previous myocardial infarction in the territories of total occlusion vessel.

Simple methods, such as the absence of Q waves on an ECG or the absence of a history of a prior MI, up to advanced imaging, such as positron emission tomography (PET) and cardiac MRI, have been used to predict which patients might have LV function improvement after revascularization.
A previous MI is a known predictor for impaired clinical outcome irrespective of reduced LV function. Presence of a CTO may, therefore, identify a subset of patients with a poor clinical outcome in the setting of ST elevation myocardial infarction (STEMI).

This study was the first to demonstrate a higher 1-year mortality rate in patients with MVD and the presence of a CTO in a non-IRA.

Recent studies have shown that patients with a CTO in non-IRAs are a subgroup of patients who are truly at risk after primary PCI is performed for STEMI.
### In-Hospital Outcomes and Complications Post PCI According to Procedural Success

<table>
<thead>
<tr>
<th>Complications</th>
<th>sCTO (n = 582)</th>
<th>uCTO (n = 254)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial complications</td>
<td>6 (1.0)</td>
<td>2 (0.8)</td>
<td>0.680</td>
</tr>
<tr>
<td>Coronary dissection</td>
<td>12 (2.1)</td>
<td>33 (12.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Side-branch occlusion</td>
<td>6 (1.0)</td>
<td>1 (0.4)</td>
<td>0.172</td>
</tr>
<tr>
<td>No/slow flow</td>
<td>2 (0.3)</td>
<td>3 (1.2)</td>
<td>0.183</td>
</tr>
<tr>
<td>Coronary Perforation</td>
<td>2 (0.3)</td>
<td>15 (5.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tamponade</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td>0.303</td>
</tr>
<tr>
<td>In-hospital adverse events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>12 (2.1)</td>
<td>8 (3.1)</td>
<td>0.393</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0.0)</td>
<td>1 (0.4)</td>
<td>0.303</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>7 (1.2)</td>
<td>4 (1.6)</td>
<td>0.861</td>
</tr>
<tr>
<td>Reintervention PCI</td>
<td>2 (0.3)</td>
<td>0 (0.0)</td>
<td>0.765</td>
</tr>
<tr>
<td>CVA</td>
<td>2 (0.3)</td>
<td>1 (0.4)</td>
<td>0.303</td>
</tr>
<tr>
<td>Emergency CABG</td>
<td>1 (0.2)</td>
<td>2 (0.8)</td>
<td>0.576</td>
</tr>
</tbody>
</table>

*Jones et al., JACC Cardio Interv 2012;5:380*

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### The high incidence of complications can result from:

- Damage of the proximal coronary artery or side branches.
- Aortic dissection.
- Impairment of collateral flow.
- Retrograde dissection with branch occlusion or perforation.
- Guide wire entrapment.
- Sub-acute vessel re-occlusion (8% in CTO Vs. 1.8% in non CTO within 24hs.
- Extensive contrast use and fluorescence time.
- Vessel perforation.
• SO, the explanation has been used traditionally for CTO PCI (that the artery is already occluded and it can not get worse, it can only get better) is not true.
• PCI for a CTO is not a low risk procedure.

Summary

• SO, in general, PCI is warranted for CTO case when:
  – The occluded vessel is responsible for the patient’s symptoms
  – PCI may also be considered in selected cases of silent ischemia if a large myocardial territory is at risk.
  – The myocardial territory supplied by the occluded artery is viable.
  – The likelihood of success is moderate to high (>60%)
THANK YOU!