1 CTO Interventions: Definition, Prevalence, Indications, Guidelines

1.1 CTO Definition

Coronary chronic total occlusions (CTOs) are defined as 100% occlusions in the coronary arteries with TIMI 0 flow of at least 3 months’ duration. The duration may be difficult to determine if there is no prior angiogram demonstrating presence of the CTO. In such cases estimation of the occlusion duration is based upon first onset of angina or dyspnea and/or prior history of myocardial infarction in the target vessel territory.

Importantly, occluded arteries within 30 days of causing a myocardial infarction, such as those included in the Open Artery Trial (OAT) do not fall within the definition of a CTO. Hence, the lack of benefit observed with percutaneous coronary intervention (PCI) in these subacute lesions should not be extrapolated to CTO patients.

1.2 Prevalence of CTOs

Coronary CTOs are common. In the best contemporary estimate of CTO prevalence at least one coronary CTO was present in 18.4% of patients with coronary artery disease among 14,439 patients undergoing coronary angiography at three Canadian centers. The CTO prevalence was higher (54%) among patients with prior coronary artery bypass graft (CABG) surgery and lower among patients undergoing primary PCI for acute ST-segment elevation myocardial infarction (10%) (Figure 1.1). Left ventricular function was normal in >50% of patients with CTO and half of the CTOs were located in the right coronary artery.

Kahn reported a CTO prevalence of 35%, while Werner et al. demonstrated a prevalence of 33% among patients with coronary artery disease (CAD) (defined as ≥50% diameter stenosis in ≥1 vessel) presenting with stable angina. Christofferson et al. reported a CTO prevalence of 52% in patients with CAD (defined as ≥70% stenosis in ≥1 vessel) among all non-CABG patients presenting for diagnostic angiography in a registry of 8004 veterans over a 10-year period.
1.3 Indications and Potential Clinical Benefits of CTO PCI

Deciding to perform CTO PCI should depend on the patient’s clinical presentation and risk benefit ratio and not the patient’s anatomy, as experienced operators using contemporary CTO PCI techniques can be expected to be successful in the great majority of patients (80–90%), even among the most complex CTO lesions. Successful CTO PCI can provide numerous benefits:

1. Improve symptoms, such as angina and dyspnea.
2. Decrease the need for CABG surgery.
3. Decrease the need for anti-anginal medications.
4. Reduce mortality (compared to patients with failed CTO PCI).
5. Improve left ventricular function.
6. Decrease the risk for arrhythmias.
7. Improve tolerance of acute coronary syndromes that may occur in the future.

1. Improved quality of life: Successful CTO PCI can decrease or eliminate angina\textsuperscript{7,8} and non-anginal\textsuperscript{9} symptoms and improve exercise capacity.\textsuperscript{10} Joyal et al.\textsuperscript{8} performed a meta-analysis comparing patients in whom CTO PCI failed to those in whom CTO PCI was successful. Patients with a successful procedure had significant reductions in recurrent angina during 6 years of follow-up (odds ratio, 0.45; 95% confidence interval, 0.30–0.67).\textsuperscript{8} Successful CTO PCI also significantly improved the patients’ functional status and quality of life.\textsuperscript{7} Apart from angina, many patients with coronary CTOs may present with dyspnea or fatigue. Patients with these manifestations of coronary ischemia are frequently miscategorized as asymptomatic, as patients get accustomed to these
symptoms and may not report them, or may minimize their severity. Many patients may also substantially curtail their physical activities and misattribute these adverse lifestyle changes to normal aging or other factors.

2. Decreased need for CABG (and offer revascularization options to patients who are poor candidates for CABG): In patients with stable coronary disease, CABG can reduce mortality and the risk of myocardial infarction in patients with very complex anatomy, whereas outcomes are similar with PCI and CABG in patients with less complex disease (Syntax score ≤ 22). Thus, CABG is the preferred revascularization modality in patients with complex coronary artery disease. However, many patients decline CABG for nonmedical reasons or because of concerns regarding complications and recovery. Other patients have increased risk for complications if they undergo CABG (e.g., patients with multiple comorbidities or patients who require redo CABG). In such cases, CTO PCI provides additional treatment options. Examples where CTO PCI is preferable to CABG include patients with single vessel right coronary artery CTO and intractable, medically refractory angina and patients with prior CABG, especially if they have a patent left internal mammary artery graft to the left anterior descending artery.

3. Decreased need for anti-anginal medications: Patients who undergo successful CTO PCI usually require fewer or no anti-anginal medications, obviating the medication-related cost and side effects. Eliminating nitrate intake can also allow patients to take phosphodiesterase inhibitors (e.g., sildenafil, vardenafil, tadalafil) for erectile dysfunction.

4. Reduced mortality: Whether CTO PCI improves survival is unproven, yet most (but not all) observational studies have shown better survival among patients with successful versus failed CTO PCI (Figure 1.2), even though bare metal stents or balloon angioplasty were used in many of those studies. In a single-center, retrospective study, mortality benefit was only observed when the CTO target vessel was the left anterior descending artery but not the right coronary artery or the circumflex (Figure 1.3).

Complete revascularization has been associated with lower risk for death, myocardial infarction, and repeat revascularization compared to incomplete revascularization. The presence of a CTO is strongly associated with incomplete revascularization, which in turn is associated with improved clinical outcomes. In a study of 301 patients who underwent myocardial perfusion imaging before and after CTO PCI, a baseline ischemic burden of >12.5% was optimal in identifying patients most likely to have a significant decrease in ischemic burden post—CTO PCI. Hence, the highest benefit of CTO PCI is more likely to be achieved in patients with significant baseline myocardial ischemia.

Well-developed collateral circulation to the CTO target vessel does not necessarily suggest that ischemia is absent. When fractional flow reserve (FFR) was performed in 92 patients immediately after CTO crossing with a microwafer but before balloon angioplasty and stenting, FFR was <0.80 in all patients. Similar findings were observed in a study of 50 CTO patients, in which all patients were ischemic regardless of the presence and extent of collateral circulation (Figure 1.4).

5. Improved left ventricular systolic function: Successful CTO revascularization can improve left ventricular systolic function, provided that the CTO-supplied myocardium is viable and the vessel remains patent during follow-up.
Figure 1.2 Impact of successful CTO revascularization on long-term survival.
Kaplan–Meier curves showing cumulative probability of all-cause mortality after PCI (A) according to procedural success and (B) comparing CTO and non–CTO PCI.

*Source:* Reproduced with permission from Ref. 15.
viability can be assessed using several techniques; however, if the affected myocardial segment is hypokinetic but not akinetic and if there are no Q-waves in the corresponding region of the electrocardiogram, then viability is highly likely.

6. **Decreased risk for arrhythmias**: Ischemia may predispose to ventricular arrhythmias. Among 162 patients with ischemic cardiomyopathy who received an implantable cardioverter defibrillator in the VACTO study, 44% had at least one CTO. During a median follow-up of 26 months, the presence of CTO was associated with higher rates of ventricular arrhythmia and death ($p < 0.01$). However, there is currently no prospective study demonstrating that CTO PCI decreases the risk for subsequent arrhythmias.

7. **Improved tolerance of a future acute coronary syndrome**: Patients with CTO who develop an acute coronary syndrome (ACS) have much worse outcomes than those who do not have a CTO including patients with multivessel coronary artery disease (Figure 1.5).
Although there are no prospective studies showing that “prophylactic” CTO PCI can improve the outcomes of future ACS, a retrospective study showed improved outcomes with successful versus failed CTO PCI after primary PCI for acute ST-segment elevation myocardial infarction (MI).

In addition to the above-mentioned patient benefits, CTO PCI also enhances the operator’s overall PCI skills and can improve the success, safety, and efficiency of non-CTO PCI cases. For example, a knuckle wire and a Stingray balloon (described in Section 2.5.2) were used to reenter into the distal true lumen.

Figure 1.4 Fractional flow reserve after CTO crossing. (A) Fractional flow reserve among 92 CTO patients demonstrating ischemia in all patients. (B) Fractional flow reserve among 50 CTO patients demonstrating ischemia in all patients, even in the presence of well-developed collaterals.

Sources: (A) Courtesy of Dr. Gerald Werner. (B): Reproduced with permission from Ref. 23.
after dissection and guidewire position loss occurred during non-CTO PCI (Figure 1.6). In another case, the Stingray balloon and wire were used to cross the culprit lesion in a patient with ST-segment elevation acute myocardial infarction. Finally, similar devices to those used in coronary CTOs are used to treat peripheral CTOs (such as the Viance catheter and Enteer balloon and guidewires, Covidien) and coronary CTO PCI experience could enhance the outcomes of peripheral arterial interventions.

1.4 Guidelines for CTO PCI

In the 2011 American College of Cardiology/American Heart Association PCI guidelines, CTO PCI carries a class IIA/level of evidence B recommendation (Figure 1.7). The guidelines emphasize the importance of selecting patients with appropriate clinical indications for CTO PCI and the importance of operator expertise.

1.5 Appropriateness Use Criteria in CTO PCI

Traditionally CTO PCI has been associated with lower success and higher procedural complication rates; hence, the appropriateness use criteria currently provide lower level recommendation for performing CTO compared to non-CTO PCI (Figure 1.8).
However, with increasing procedural success and decreasing major complication rates with the use of contemporary CTO PCI techniques (Figure 1.9), the appropriateness use criteria for CTO PCI will likely be revised to reflect those advances.

Figure 1.6 Example of CTO techniques application for the treatment of non–CTO lesions. Coronary angiography demonstrating a tortuous right coronary artery with a proximal (arrow, A) and mid (multiple arrows, A) lesions. Mid right coronary artery dissection after balloon predilation (arrow, B). Guidewire position and antegrade flow were lost after an unsuccessful attempt for stent delivery. After failure to advance a guidewire through the dissected segment, a knuckle was formed with a Pilot 200 guidewire (Abbott Vascular) (arrow, C) and advanced around the dissected segment. Using a Stingray balloon (Bridgepoint Medical) (arrows, D) and guidewire distal true lumen re-entry was achieved (D). Using a Guideliner catheter (Vascular Solutions, Minneapolis, MN) (arrow, F) two stents were successfully delivered with an excellent final angiographic result (G).

Source: Reproduced with permission from Ref. 40.

Figure 1.7 Current guideline recommendation for CTO PCI.
Figure 1.8  Appropriateness use criteria for PCI highlighting categories (10 of 36) in which CTO PCI carries lower recommendation than non—CTO PCI.  
Source: Modified with permission from Ref. 43.

Figure 1.9  Meta-analysis of procedural success and complication rates of CTO PCI over time, demonstrating increasing success and decreasing complication rates.  
Source: Modified with permission from Ref. 44.
1.6 Contraindications to CTO PCI

Absolute contraindications:
1. Inability to receive dual antiplatelet therapy (e.g., due to bleeding diathesis). Patients with contraindications to dual antiplatelet therapy are best treated with CABG surgery.
2. Prior radiation skin injury.

Relative contraindications:
1. Inability to receive prolonged dual antiplatelet therapy required after drug-eluting stent implantation, given the high restenosis rates with bare metal stents in CTOs (as described in Chapter 11).
2. Chronic kidney disease, as high contrast volume may be needed during the procedure (however, contrast use can be minimized using intravascular ultrasonography for PCI guidance or using the retrograde approach).
3. Prior radiation exposure, or multiple and prolonged prior cardiac procedures requiring fluoroscopy, given the increased risk for radiation skin injury with repeat X-ray exposure.
4. Heparin-induced thrombocytopenia (although bivalirudin could potentially be used in such cases).

1.7 Summary and Conclusions

In summary, CTO PCI can provide significant patient benefits when clinically indicated. In symptomatic patients, the myocardium supplied by a CTO is always an ischemic zone, even with well-developed collateral circulation. Continued ischemia is associated with worse clinical outcomes, and successful CTO PCI is important for achieving complete coronary revascularization. How to successfully and safely perform CTO PCI will be discussed in detail in the following chapters.

References


