**Guiding Principles for Chronic Total Occlusion Percutaneous Coronary Intervention: A Global Expert Consensus Document**

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**ABSTRACT**

Outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has improved due to advancements in equipment and techniques. With global collaboration and knowledge sharing, we have identified 7 common principles that are widely accepted as best practices for CTO-PCI.

1. Symptom improvement is the primary indication for CTO PCI.
2. Dual coronary angiography and in-depth and structured review of the angiogram (and, if available, coronary computed tomography angiography) are key for planning and safely performing CTO-PCI.
3. Use of a microcatheter is essential for optimal guidewire manipulation and exchanges.
4. Antegrade wiring, antegrade dissection and re-entry and the retrograde approach are all necessary crossing strategies. Antegrade wiring is the most common initial technique, while retrograde and antegrade dissection and re-entry are often required for complex CTOs.
5. If the initially selected crossing strategy fails to achieve progress, efficient change to an alternative crossing technique increases the likelihood of eventual PCI success, shortens procedure time, and lowers radiation and contrast use.
6. Specific CTO-PCI expertise and volume and the availability of specialized equipment will increase the likelihood of crossing success and facilitate prevention and management of complications, such as perforation.
7. Meticulous attention to lesion preparation and stenting technique, often requiring intracoronary imaging, is required to ensure optimum stent expansion and minimize the risk of adverse events.

The above principles have been widely adopted by experienced CTO-PCI operators and centers currently achieving high success and acceptable complication rates. Outcomes are less optimal at less experienced centers, highlighting the need for more widespread adoption of the aforementioned seven guiding principles along with the development of additional simple and safe CTO crossing and revascularization strategies through ongoing research, education and training.

**Keywords:** Chronic total occlusion, percutaneous coronary intervention, techniques, outcomes

**CONDENSED ABSTRACT**

We present seven globally-supported key principles for chronic total occlusion (CTO) percutaneous coronary intervention (PCI). First, symptom improvement remains the most common clinical goal. Second, dual coronary angiography and thorough, structured angiogram review are essential. Third, a microcatheter should be used to support the guidewire. Fourth, antegrade wiring, antegrade dissection and re-entry and the retrograde approach are important CTO crossing strategies. Fifth, changes between crossing strategies should be made efficiently if the initial approach fails to achieve progress. Sixth, specific CTO-PCI expertise and equipment, including for complication management, should be available. Seventh, meticulous attention to lesion preparation and stenting technique can help minimize the risk of adverse events.

**Abbreviations and Acronyms**

BASE, balloon-assisted subintimal entry

CCTA, coronary computed tomography angiography

CTO, chronic total occlusion

IVUS, intravascular ultrasound

PCI, percutaneous coronary intervention

Chronic total occlusions (CTOs) are completely occluded arteries with Thrombolysis In Myocardial Infarction (TIMI) 0 flow with an estimated duration of at least 3 months. In recent years the success rates of CTO percutaneous coronary intervention (PCI) have substantially improved, in concert with the maturation and refinement of the key indications, equipment, and techniques for recanalization of occluded coronary arteries. In recent years CTO percutaneous coronary intervention (PCI) has evolved significantly, along with gradual maturation and refinement of the key indications, equipment, and techniques. Global collaboration and sharing of knowledge and techniques have led to the emergence of seven key principles for the performance of CTO-PCI that can help training, clinical practice, and education in this field (**Table 1**).

This document was conceived during CTO-PCI meetings in 2018 (CTO Summit, Multi-Level CTO, and Euro-CTO). An initial document draft was created by a group of CTO-PCI experts from North America, Europe, and Japan. A total of 113 CTO-PCI experts from 56 counties were invited to participate of whom 101 from 50 countries provided comments and approved the final document.

1. **Symptom improvement is the primary indication for CTO-PCI**

Two published randomized-controlled clinical trials 1, 2 and several observational studies 3 have reported symptom improvement after successful CTO-PCI. The EuroCTO (A Randomized Multicentre Trial to Evaluate the Utilization of Revascularization or Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions) multicenter trial randomized 407 patients to CTO-PCI vs. optimal medical therapy alone. At 12 months, compared with patients randomized to medical therapy only, patients randomized to CTO-PCI had greater improvement in angina frequency [subscale change difference: 5.23, 95% confidence interval (CI) 1.75-8.71; p=0.003], and quality of life (subscale change difference: 6.62, 95% CI 1.78-11.46; p=0.007), as assessed with the Seattle Angina Questionnaire 1. The single center IMPACTOR-CTO (Impact on Inducible Myocardial Ischemia of PercutAneous Coronary InTervention versus Optimal Medical TheRapy in Patients with Right Coronary Artery Chronic Total Occlusion) trial randomized 94 patients with isolated right coronary artery CTO to CTO-PCI vs optimal medical therapy alone 2. At 12 months, compared with optimal medical therapy, CTO-PCI patients had a significant reduction in ischemic burden and improvement in six-minute walk distance and quality of life as assessed by the short Form-36 Health Survey. Such symptomatic improvement confirms results from multiple observational studies and meta-analyses 4-6. Interpretation of randomized CTO-PCI trials should take into consideration selection bias, since the most symptomatic patients were less likely to be enrolled, as well as crossover between arms. For example, no symptomatic benefits were observed in a third randomized trial, DECISION CTO (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion (presented at the 2017 American College of Cardiology annual meeting). However this study enrolled patients with minimal symptoms in both arms, and crossover rates were high in both treatment arms, randomizing the outcomes toward the null. In addition, no sham-controlled trial has yet been performed, leaving the possibility that some of the observed benefit of CTO-PCI is mediated by the placebo effect. One such trial is underway (SHam-controlled INtErvention to Improve QOL in CTOs - SHINE-CTO; NCT02784418).

In observational studies CTO-PCI relieved regional ischemia 7, and has been associated with improved exercise capacity, increased anaerobic threshold 8, and improvement in depression 9. Viable myocardium supplied by a CTO is a persistently ischemic zone 10, 11. It remains undetermined whether CTO-PCI improves other cardiovascular outcomes, such as left ventricular ejection fraction, risk for arrhythmias, and mortality. Both regional and global left ventricular function improved after successful CTO-PCI in several carefully performed observational studies 12 using paired cardiac magnetic resonance imaging in patients with demonstrable viability or baseline dysfunction 13, but not in two randomized-controlled trials 14, 15. These randomized studies, however, did not examine the presence of viable dysfunctional myocardium at baseline, nor did they assess exercise induced changes in left ventricular function 16. In patients with ischemic cardiomyopathy with reduced ejection fraction, the presence of ischemia and viability in the myocardium supplied by the CTO vessel should be confirmed before considering CTO revascularization. Patients with coronary CTOs who received an implantable cardioverter defibrillator for primary or secondary prevention, had a higher risk for ventricular arrhythmias than patients with non-occlusive coronary artery disease 17, 18 and a higher frequency of recurrent ventricular tachycardia after ablation 19; there been no randomized studies, however, examining whether CTO-PCI reduces the risk for subsequent arrhythmias. In observational studies, patients presenting with ST-segment elevation acute myocardial infarction and a CTO in a non-culprit coronary artery had higher risk for developing cardiogenic shock and higher mortality 20-22.

In a meta-analysis of successful vs. failed CTO-PCI, patients with successful procedures had lower mortality compared with those who had unsuccessful procedures, but findings based on observational studies are subject to bias 4. Observational studies have also demonstrated a lower incidence of major adverse cardiac events with CTO-PCI 23, 24 as compared with medical therapy alone, even among patients with well-developed collateral circulation 25. Although CTO-PCI may improve “hard outcomes”, especially in patients with large ischemic burden (e.g. ischemia of >10% of the myocardium) in whom complete revascularization is achieved 26-28, this hypothesis will require confirmation in well designed, prospective, randomized-controlled clinical trials, such as the ongoing Nordic and Spanish Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy of Chronic Total Coronary Occlusions With Myocardial Ischemia (ISCHEMIA-CTO, [NCT03563417](https://clinicaltrials.gov/show/NCT03563417)) and the NOrdic-Baltic Randomized Registry Study for Evaluation of PCI in Chronic Total Coronary Occlusion (NOBLE-CTO, [NCT03392415](https://clinicaltrials.gov/show/NCT03392415)).

In summary, improving patient symptoms caused by myocardial ischemia (angina, exertional dyspnea, and sometimes fatigue) despite optimal medical therapy remains the only benefit of CTO-PCI that has been demonstrated in randomized-controlled trials and should therefore currently be the primary indication for offering this procedure to patients. The procedural benefit will likely be proportional to symptoms severity, thus an office-based risk-benefit conversation with prospective CTO-PCI patients is strongly encouraged to provide realistic expectations prior to the procedure.

1. **Dual angiography and detailed, structured angiographic review**

The simplest, yet most powerful, technique for improving technical success and reducing complications of CTO-PCI is the performance of high quality, simultaneous dual coronary angiography. The use of two catheters and pressure systems adds little time and cost to the procedure. Dual coronary angiography allows better visualization and understanding of CTO anatomy and is pivotal in estimating the complexity of the lesion and the likelihood of success. Moreover, it improves procedural safety by elucidating the guidewire location during crossing attempts and facilitating management of periprocedural complications, such as perforation. CTO-PCI with a single guide can be done in selected cases with collateral circulation exclusively coming from ipsilateral vessels, for example in CTOs located in a left dominant system 29. In the latter scenario, selective contrast injection in the collateral donor branch through a microcatheter can be performed to reduce contrast administration. Even in the later scenario, use of 2 catheters in the left main will allow for easier guidewire and microcatheter management, especially when using a retrograde approach.

Prior to the procedure, a detailed review and analysis of the angiogram and, if available, coronary computed tomography angiography is essential for creating a primary and secondary procedural plan and assessing the risk / benefit ratio of the procedure. To allow adequate time for procedural planning and preparation ***ad hoc* CTO-PCI should be discouraged** in most cases. CTO-PCI pre-planning can also help minimize contrast and radiation dose, reduce patient and operator fatigue, allow additional evaluation (such as myocardial viability) to be performed, and enable detailed discussion with the patient about all the aspects of the CTO-PCI procedure.

CTO anatomy will dictate the most likely successful and safest crossing strategies. Angiographic review of the CTO anatomy focuses on 4 characteristics: (1) proximal cap morphology; (2) occlusion length, course, and composition (e.g. calcium); (3) quality of the distal vessel; and (4) characteristics of the collateral circulation. Moreover, non-CTO lesions are reviewed, as assessing intermediate left main or other lesions may change clinical decision making leading to alternative revascularization strategies, such as coronary artery bypass graft surgery or pre-CTO-PCI stenting of a donor artery.

**2.1 Proximal cap morphology**

Determining the location and morphology of the proximal cap is critical for selecting an optimal approach to CTO-PCI. Attempts to cross ambiguous proximal caps may lead to perforation. Additional angiographic projections using dual injection, selective contrast injection through a microcatheter located near the proximal cap, use of intravascular ultrasound (IVUS) 30, or pre-procedural or real-time coronary computed tomography angiography co-registration 31 may help clarify the location of the proximal cap 32. If proximal cap ambiguity cannot be resolved, a retrograde approach is often recommended as primary strategy.

When operators are facile with the antegrade and dissection reentry technique and have access to proper equipment for reentry, subintimal techniques such as balloon-assisted subintimal entry (BASE, i.e. inflation of a balloon proximal to the occlusion to cause a dissection, followed by subintimal guidewire entry and subintimal crossing of the occlusion) may be used 33.

* 1. **Lesion length, course, and composition**

Lesion length is often overestimated with antegrade only injections due to under filling and poor opacification of the distal vessel, from competing antegrade and retrograde coronary flow, leaving uncertainty about the location and morphology of the distal cap. Dual injection allows more accurate estimation of CTO length and the distal cap anatomy. Severe calcification and tortuosity of the occluded segment can hinder CTO crossing and increase the likelihood of subadventitial guidewire entry. Advancing a knuckled (J-shaped) guidewire or changing to the retrograde approach is often preferred when the vessel course is unclear or highly tortuous 34, as such a wire shape allows advancement within the vessel architecture with low risk of perforation 35.

* 1. **Distal vessel**

A distal vessel that fills well, does not have significant disease and is free from major branches facilitates CTO recanalization. Conversely, small, diffusely diseased distal vessels are more challenging to recanalize, especially following subintimal guidewire entry. In some cases, however, distal vessels are small due to hypoperfusion, leading to negative remodeling and will increase in size after recanalization 36. Distal CTO caps in native coronary artery CTOs are more likely to be calcified and resistant to guidewire penetration in prior CABG patients 37. Moreover, distal vessel calcification may hinder wire re-entry in case of subintimal guidewire entry. The presence of a bifurcation at the distal cap (as well as at the proximal cap or within the occluded segment) may hinder antegrade wiring of the main branch and also increases the likelihood of side branch loss, favoring use of the retrograde approach.

* 1. **Collateral circulation**

Evaluation of the collateral circulation is critical for determining the feasibility of the retrograde approach 38. High quality angiography (ideally obtained in apnea and without panning) allowing complete opacification of collateral vessels and obtained in optimal angiographic projections, should therefore be encouraged as part of routine diagnostic studies when a CTO is found. Retrograde access to the distal vessel can be obtained via septal collaterals, epicardial collaterals, or (patent or occluded) coronary bypass grafts. When assessing collateral channels it is important to consider size, tortuosity, angle of entry to and exit from the collateral, and distance from the collateral exit to the distal cap. The most important predictor of successful guidewire and device crossing is lack of tortuosity, followed by size 39. The size of the collaterals is often assessed using the Werner classification 10. In addition, crossing invisible septal collateral channels is often possible with the surfing technique, letting the wire find the path of least resistance 40. It is helpful to carefully study previous angiograms for multiple potential collateral pathways, as the predominant collateral may change over time prior to the procedure or during the course of PCI (“shifting collaterals”). Previously visualized collaterals that disappear at the time of the procedure may still be crossable. Whenever required and after ensuring adequate backflow to prevent barotrauma, selective contrast tip injections through the microcatheter can be safely performed to outline collateral anatomy. Patent bypass grafts represent an ideal retrograde conduit due to the absence of side branches, predictable course and large caliber. Even occluded grafts can be used as retrograde pathways. Septal collaterals are typically safer and easier to navigate using very soft tip and polymer-jacketed guidewires compared with epicardial collaterals 41, 42. In contrast to epicardial collaterals, septal collaterals can be safely dilated with small balloons to facilitate microcatheter or device crossing if required. The donor vessel proximal to the collateral origin, as well as collateral dominance (ie. presence of a single large visible collateral), should also be assessed during retrograde procedures to determine the risk for ischemia during retrograde crossing attempts. Careful review of collaterals prior to the procedure can reduce contrast and radiation dose as well as the duration of the procedure. In cases where the collateral anatomy is unclear or ambiguous, it can be helpful to perform selective injection of contrast into the collateral through the center lumen of a microcatheter placed into the collateral using a 2-3 cc syringe. Furthermore, in cases where unfavorable non-interventional epicardial collaterals provide the dominant blood flow to the CTO, it can be useful to balloon occlude the epicardial collateral for 2-4 minutes to see if more favorable interventional collaterals can be recruited and identified for attempts at retrograde crossing.

* 1. **CTO scores**

Angiographic and clinical characteristics, such as prior CTO-PCI failure 43 and prior CABG 44, have been combined to create scores for estimating the difficulty and hazard of a specific CTO-PCI in various patient populations. The first and most commonly used CTO-PCI score is the J-CTO score (Multicenter CTO Registry of Japan), developed to estimate the likelihood of successful antegrade guidewire crossing within 30 minutes based on 5 criteria (at least 1 bend of >45° in the CTO entry or CTO body, occlusion length >20 mm, calcification, blunt proximal stump, and previously failed attempt) 45. The J-CTO score has been validated in other CTO-PCI cohorts 43 and is also associated with 1-year clinical outcomes 46. Other scores include the PROGRESS-CTO score 47, the RECHARGE (**RE**gistry of **C**rossboss and **H**ybrid Procedures in Fr**A**nce, the Nethe**R**lands, Bel**G**ium and Unit**E**d Kingdom) registry score 48, the CL-score [**C**linical and **L**esion related score) 49, the ORA (**o**stial location, collateral filling of **R**entrop <2, **a**ge over 75) score 50, the Ellis et al. score 51, the weighted angiographic scoring model (W-CTO score) 52, and the CASTLE (**C**ABG history, **A**ge (≥70yrs), **S**tump anatomy (blunt or invisible), **T**ortuosity degree (severe or unseen), **L**ength of occlusion (≥20 mm) and **E**xtent of calcification (severe)] score 53. There are also CCTA-based scores, such as the CT-RECTOR multicenter registry (Computed Tomography Registry of Chronic Total Occlusion Revascularization) score 54 and the Korean Multicenter CTO CT Registry Score 55. Various scores have similar predictive capacity for technical success and are more accurate in antegrade-only cases 56. Risk of complications can also be predicted using the Progress-CTO complications score which uses 3 variables (age ≥ 65 years, lesion length > 23 mm, and use of the retrograde approach) to stratify patients for the risk of periprocedural complications 57. Each score is generally only applicable to the population from which it was derived and validated. Calculating one or more scores can promote detailed review of the angiogram and facilitate decision making. For example, medical therapy may be preferred over CTO-PCI in mildly symptomatic patients with highly complex occlusions. Complex CTOs (such as those with J-CTO score ≥2) are more likely to require dissection re-entry and retrograde crossing techniques and should be performed by experienced operators.

1. **Use of a microcatheter for guidewire manipulation**

A microcatheter should be routinely used for supporting the coronary guidewire and allowing rapid guidewire switching during both antegrade and retrograde wire manipulation. Microcatheters improve the precision of both rotational and longitudinal guidewire movements both in fluid (blood filled vessels) and in tissue (the occlusion itself) and allow the penetration force of the wire to be dynamically altered by changing the distance between the tip of the guidewire and the microcatheter, with microcatheters becoming stiffer when the microcatheter is positioned close to the guidewire tip. Microcatheters also allow rapid guidewire tip reshaping or exchange, while preserving prior guidewire crossing or advancement achieved. Microcatheters inherently dilate retrograde collateral channels and protect them from wire-induced trauma. Microcatheters can also be used to deliver contrast either for visualization or to accomplish the Carlino technique (intra-lesional injection of 1-2 mL of contrast to elucidate microcatheter position and/or facilitate crossing), especially in wire resistant lesions 58. A microcatheter is preferred over an over-the-wire balloon as it has a marker at the distal tip, providing adequate fluoroscopic feedback of its actual position and also provides greater freedom of advancement with a lower profile and better wire to lumen internal diameter ratio. Also, unlike over-the-wire plastic balloon catheter shafts that are prone to kinking, nearly all contemporary coronary microcatheters incorporate a kink-resistant metallic braid.

Several microcatheters are currently available. Microcatheters utilized in CTO-PCI can be broadly classified into 4 categories: (a) larger microcatheters, often with threaded external surfaces, that provide stronger support; (b) lower profile, flexible microcatheters optimized for advancing through microchannels and collaterals; (c) dual lumen microcatheters that can facilitate parallel wiring and wiring of bifurcated lesions; and (d) angulated microcatheters that can facilitate wire advancement around acute angles.

Similar to guidewires, microcatheter selection depends on the CTO angiographic characteristics, local availability, and expertise. In addition to using a microcatheter, obtaining coaxial guide position and strong guide support can significantly facilitate CTO crossing.

1. **CTO crossing strategies**

There are 4 CTO crossing strategies, classified according to wiring direction (antegrade and retrograde) and whether or not the subintimal space is utilized (wiring vs. dissection and re-entry).

**4.1 Antegrade wiring**

Antegrade wiring (also called antegrade wire escalation) is the most widely used CTO crossing technique 30, 59-61. Various guidewires are advanced in the antegrade direction (original direction of blood flow). Guidewire choice depends on CTO characteristics. If there is a tapered proximal cap or a functional occlusion with a visible channel, a polymer-jacketed, low penetration force, tapered guidewire is used initially, with subsequent escalation to intermediate and high penetration force guidewires, as required. If there is a blunt proximal cap, antegrade wiring is usually started with an intermediate penetration force polymer-jacketed guidewire, or a composite core guidewire. Stiff, high penetration force guidewires may be required in highly resistant proximal caps or when areas of resistance are encountered within the body of the occlusion. After proximal cap crossing, however, de-escalation to less penetrating guidewires should be done for navigation through the CTO segment.

Contralateral injection and orthogonal angiographic projections are critical for determining guidewire position during crossing attempts. If the guidewire enters into the distal true lumen, the microcatheter is then advanced into the distal true lumen and the dedicated CTO guidewire is then exchanged for a workhorse guidewire through the microcatheter to minimize the risk for distal vessel injury and perforation during balloon angioplasty and stenting (wire de-escalation). If the guidewire exits the vessel structure it should be withdrawn and re-directed **without** advancing microcatheters, balloons, or stents over it. If the guidewire enters the subintimal space it can be redirected, but if this maneuver fails, the wire can be left in place to aid directing a second guidewire into the distal true lumen (parallel wire technique), which can be assisted by a dual lumen microcatheter, or facilitated by the use of IVUS 30. Alternatively, antegrade dissection/re-entry techniques can be used to re-enter into the distal true lumen, as described below. Subintimal guidewire advancement distal to the distal cap should be avoided as it can lead to hematoma formation, causing luminal compression and reducing the likelihood of success. Antegrade vessel re-entry can be guided by IVUS, although this approach requires expertise and may by hindered by limited wire maneuverability in the presence of the subintimal IVUS catheter.

* 1. **Antegrade dissection and re-entry**

Antegrade dissection and re-entry involves entering the subintimal space, followed by subintimal crossing of the CTO with subsequent re-entry into the distal true lumen. Antegrade dissection and re-entry may be intentional or un-intentional during antegrade wiring attempts. The first dissection re-entry technique developed was named STAR (**S**ubintimal **T**racking **A**nd **R**e-Entry) and used inadvertent, poorly controllable re-entry into the distal lumen 62. This frequently necessitated stenting long coronary segments with occlusion of numerous side branches, with extensive vascular injury with high rates of in-stent restenosis and re-occlusion. As such, the STAR technique has evolved to a bailout strategy without stent implantation after ballooning, in preparation for a repeat CTO-PCI attempt (subintimal plaque modification, also termed an “investment” procedure) 62-65. The development of limited dissection/re-entry techniques (using dedicated re-entry systems 66, 67 or wire based strategies 68, 69) was an important advance, as they minimize vascular injury, limit the length of dissection and subsequent stent length, and increase the likelihood of side branch preservation 35, 66, 70. Such approaches have been associated with favorable clinical outcomes 70-74.

* 1. **The retrograde approach**

The retrograde technique differs from the antegrade approach in that the occlusion is approached from the distal vessel with guidewire advancement against the original direction of blood flow 75. A guidewire is advanced into the artery distal to the occlusion through a collateral channel or through a bypass graft, followed by placement of a microcatheter at the distal CTO cap. Retrograde CTO crossing is then attempted either with retrograde wiring [usually for short occlusions, especially when the distal cap is tapered 37] or using retrograde dissection/re-entry techniques.

The most commonly used retrograde crossing technique is reverse controlled antegrade and retrograde tracking (reverse CART), in which a balloon is inflated over the antegrade guidewire, followed by retrograde guidewire advancement into the space created by the antegrade balloon. In challenging reverse CART cases, intravascular ultrasound can clarify the mechanism of failure and increase the likelihood of success 76. Guide catheter extensions can also facilitate reverse CART 77.

* 1. **Crossing strategy selection**

Selecting the initial and subsequent crossing strategies depends on the CTO lesion characteristics and local equipment availability and expertise.

Several algorithms have been developed to facilitate crossing strategy selection, such as the hybrid 78 and Asia Pacific 34 algorithm. Antegrade crossing is generally preferred over retrograde crossing as the initial crossing strategy, given the higher risk of complications with the retrograde approach 59-61 and need for antegrade lesion preparation even when the retrograde approach is eventually required. Some retrograde CTO-PCI complications, however, are caused by antegrade crossing attempts. The retrograde approach remains critical for achieving high success rates, especially in more complex CTOs 61, 79, and has been associated with favorable long-term outcomes 80.

CTOs with proximal cap ambiguity and flush aorto-ostial CTOs are often approached with a primary retrograde approach. Alternatively, they can be approached in the antegrade direction, especially when no collateral or graft can be used by using: (a) using intravascular ultrasound or pre-procedural computed tomography coronary angiography for determining the location of the proximal cap and vessel course 31, 34, 81, or (b) techniques to facilitate entry into the subintimal space proximal to the occlusion 33.

1. **Change of crossing strategy**

Flexibility is important for the success, safety, and efficiency of CTO-PCI. If the initial or subsequent crossing strategy fails to achieve progress, small changes (such as modifying the guidewire tip angulation or changing guidewire) or more significant changes (such as converting from an antegrade to a retrograde approach) should be made, based on pre-procedural planning. It is important to avoid getting “stuck in a failure mode”, in which excessive time, radiation and contrast are expended with little or no progress being made while repeatedly attempting the same technique, as this will preclude the use of alternative strategies and increase the risk of complications.

Similar to selection of the initial crossing strategy, the timing and choice of subsequent crossing strategies depends on lesion characteristics, challenges encountered with the original technique, and equipment availability and expertise, and can be guided by existing crossing algorithms 34, 78. Only approximately 50-60% of CTOs are successfully crossed with the initial strategy 29, 59, 60. Changing strategies can help maximize the likelihood of eventual success and limit contrast volume and radiation dose.

Reasons to stop a CTO-PCI attempt include occurrence of a complication, high radiation dose (usually >5 Gray air kerma dose in the absence of lesion crossing or substantial progress), large contrast volume administration, exhaustion of crossing options, or patient or physician fatigue. As with all interventions, careful assessment of individual risk vs. benefit should guide decision-making and choice of strategy during different stages of the procedure. On many occasions, it may be best to fail rather than pursue highly aggressive strategies that may lead to serious complications 59.

1. **Equipment and physician team expertise**

CTO-PCI should be performed within dedicated programs that promote continual training and rigorous monitoring of outcomes.{Karmpaliotis, 2013 #3586} Higher CTO PCI volume has been associated with higher success rates.{Brilakis, 2015 #4752}{Ellis, 2017 #6280}{Kinnaird, 2018 #6610}

The performance of CTO-PCI by a skilled physician and team is especially important to minimize and manage procedural complications. CTO-PCI carries increased risk of complications compared with non-CTO-PCI 82, especially perforation, which occurred in all fatal events in a contemporary multicenter registry 3. Across multiple contemporary registries, tamponade occurred in 0.4 to 1.3% of cases **(Table 2).** Guidewire perforation within the CTO segment infrequently results in clinically significant pericardial bleeding. In contrast, balloon or microcatheter advancement outside the vessel architecture is significantly more likely to result in intra-myocardial or pericardial bleeding, leading to tamponade, or loculated hematoma, often called “dry” tamponade. Additional CTO-PCI adverse events include access site complications, donor vessel injury, arrhythmias, stroke, contrast induced nephropathy, radiation dermatitis, emergency coronary bypass graft surgery, and death 83. The average complication risk is approximately 3%, but varies widely between studies (**Table 2**) and is increased with greater lesion complexity 3, 59-61, 84, 85.

Dual injection minimizes the risk for perforation by helping determine guidewire position. Placement of a “safety” guidewire in the CTO donor vessel can facilitate treatment if donor vessel injury occurs. Maintaining an activated clotting time (ACT) of ≥300 seconds reduces the risk of donor vessel thrombosis; the ACT should be checked at least every 30 minutes during the procedure. In case of perforation, covered stents and coils should be available to treat large vessel and distal vessel perforations, respectively. Pre-procedural operator training in proper use of these devices will ensure efficient use in the emergency setting. In case of epicardial collateral perforation 42, 86 embolization from both directions (using coils, thrombin, fat, etc) is often needed to achieve sealing 87. Special attention should be given to patients with prior coronary bypass graft surgery, as perforation can result in life-threatening, difficult to access, loculated hematomas 88, 89.

Meticulous attention should also be paid to minimizing radiation dose and the risk for radiation skin injury. This can be achieved by using low-frame rate fluoroscopy and the “fluoroscopy store” function for documenting balloon and stent inflation instead of cine-angiography, using collimation, minimizing the distance of the image receptor from the patient, and intermittently changing the position of the image receptor during the procedure. Similarly, contrast administration should be minimized through meticulous pre-procedural planning and use of contrast-sparing devices to reduce the risk for contrast nephropathy.

1. **Optimal stent deployment**

CTOs often have large plaque burden and often contain calcific segments that may offer resistance to optimal stent expansion absent good preparation. As such, efforts should be made to predilate the segment with properly sized balloons, and use of atherectomy may be required. It is essential to achieve full lesion expansion before stent implantation. CTO-PCI often involves placement of multiple stents in vessels that are calcified, diffusely diseased and negatively remodeled. Given the often arduous and lengthy attempts required for CTO crossing, less attention may be given to stent optimization (maximal stent expansion and optimal inflow and outflow), potentially resulting in higher rates of restenosis and stent thrombosis. Intravascular imaging can facilitate assessment of vessel size and calcification prior to stenting and the adequacy of stent expansion, apposition and lesion coverage, to reduce the risk for subsequent adverse events 90-93. Moderate diffuse disease distal to the CTO often does not require treatment, as the distal vessel often enlarges over time after restoring vessel patency 94.

Routine high-pressure post-dilation 90, 91 of adequate duration may help optimize acute stent expansion and improve long-term outcomes. However, caution should be used when ballooning heavily calcified coronary segments or areas of subintimal crossing, as they may carry increased risk for perforation. Use of intravascular imaging can reduce the likelihood of stent oversizing and the risk for perforation.

**Conclusions**

Extensive interactions and collaboration across the world have led to the advancements in CTO-PCI that are summarized in the seven key principles outlined in this global expert consensus document. These principles can guide training of new CTO-PCI operators and program development and facilitate further improvement in the success, safety, and clinical outcomes of CTO-PCI.

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**Table 1**. Key principles on the indications and technique of chronic total occlusion percutaneous coronary intervention.

|  |  |
| --- | --- |
| 1 | The principal indication for CTO-PCI is to improve symptoms |
| 2 | Dual coronary angiography and thorough, structure angiographic review |
| 3 | Use of a microcatheter for guidewire support |
| 4 | There are 4 CTO crossing strategies: antegrade wire escalation, antegrade dissection/re-entry, retrograde wire escalation, and retrograde dissection/re-entry |
| 5 | Change of equipment and technique increases the likelihood of success and improves the efficiency of the procedure |
| 6 | Centers and physicians performing CTO-PCI should have the necessary equipment, expertise and experience to optimize success and minimize and manage complications |
| 7 | Every effort should be made to optimize stent deployment in CTO PCI, including the frequent use of intravascular imaging |

**Table 2**. Contemporary series of chronic total occlusion percutaneous coronary intervention.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Acronym** | **Study Period** | **Centers** | **Cases** | **Technical Success** | **Procedural Success** | **Overall MACE** | **Death** | **Acute MI** | **Stroke** | **TVR** | **Tamponade** |
| **Habara et al. 85** | **Japanese Retrograde Summit Registry** | 2012–2013 | 56 | 3,229 | — | 88% | 0.5% | 0.2% | 0.1% | 0.1% | — | 0.3% |
| **Tajti et al. 59** | **PROGRESS-CTO** | 2012–2017 | 20 | 3,055 | 87% | 85% | 3.0% | 0.3% | 0.7% | 0.1% | 0.2% | 0.5% |
| **Suzuki et al. 30** | **Japanese CTO-PCI Expert Registry** | 2014–2015 | 41 | 2,846 | 90% | 89% | <2% | 0.2% | 1.2% | 0.2% | 0.2% | 0.4% |
| **Maeremans et al. 60** | **RECHARGE** | 2014–2015 | 17 | 1,253 | 89% | 86% | 2.6% | 0.2% | 0.2% | 2.2% | 0.1% | 1.3% |
| **Wilson et al. 61** | **UK Hybrid** | 2012–2014 | 7 | 1,156 | 90% | — | 1.6% | 0.0% | 0.8% | 0.4% | 0.0% | 0.7% |
| **Sapontis et al. 3** | **OPEN-CTO** | 2013–2017 | 12 | 1,000 | 86% | 85% | 7.0% | 0.9% | 2.6% | 0.0% | 0.1% | — |

The studies are listed according to patient enrollment.

PROGRESS-CTO: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention

RECHARGE: REgistry of Crossboss and Hybrid procedures in FrAnce, the NetheRlands, BelGium and UnitEd Kingdom

UK hybrid: United Kingdom hybrid registry

OPEN CTO: Outcomes, Patient Health Status and Efficiency in Chronic Total Occlusion Hybrid Procedures

MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization.