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Chronic Total Occlusion Percutaneous Coronary Intervention: Present and Future

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ABSTRACT: Chronic total occlusion percutaneous coronary intervention has evolved into a subspecialty of interventional cardiology. Using a variety of antegrade and retrograde techniques, experienced operators currently achieve success rates of 85% to 90%, with an incidence of major periprocedural complications of ≈2% to 3%. Several developments in equipment (new microcatheters and guidewires, novel reentry devices), imaging (computed tomography angiography guidance, intravascular imaging for reentry), techniques (intraocclusion contrast injection, advanced subintimal tracking and reentry), and artificial intelligence (automated computed tomography image analysis and prediction of the likelihood of crossing success with various techniques) could further improve outcomes. Global collaboration and rapid dissemination of new developments accelerate the pace of progress. While innovation is exciting and necessary, adhering to the basic principles of chronic total occlusion percutaneous coronary intervention (such as continual assessment of risks and benefits, meticulous angiographic review, and use of dual injection) remains critical for achieving optimal patient outcomes.

Key Words: artificial intelligence ■ cardiology ■ coronary occlusion ■ incidence ■ risk assessment

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) can be challenging to perform, requires extensive operator training, and, similar to the treatment of other complex coronary lesions, carries a higher risk of complications compared with non-CTO PCI.[1] At the same time, it can provide substantial clinical benefits, often for patients who do not have other treatment options.[2]

CTO PCI: WHERE ARE WE NOW?

The field of CTO PCI is currently mature.[3] Improving patient symptoms is established as the key indication (Table).[2] Most CTO PCI techniques are well-defined and teachable, with several experienced operators and training programs around the world. Both antegrade and retrograde techniques are currently successfully used. A global CTO crossing algorithm[4] was developed to assist with crossing strategy selection (Figure 1). Intravascular imaging and CCTA (pre- and intraprocedural)[5] are increasingly being used to plan the procedure, cross the occlusion, and optimize the final result.[6] Drug-eluting stents are implanted in most procedures with a low incidence of target lesion revascularization and stent thrombosis.[7] Definitions of techniques and outcomes of CTO PCI have been standardized.[8]

However, there are multiple areas in need of improvement. First, there are limited clinical studies on both indications and techniques.[9] Second, most CTO PCIs are still being performed by less experienced operators with suboptimal outcomes.[1] Third, the success rates could further increase, and the complication rates could decrease. Fourth, the efficiency (ie, procedural time, radiation dose, and contrast volume) of the procedure could improve through an algorithmic approach and the use of novel equipment and techniques.[10] Fifth, imaging (noninvasive and intracoronary) remains underutilized for procedural planning and result optimization. Sixth, long-term outcomes could further improve.

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Nonstandard Abbreviations and Acronyms

CABG	coronary artery bypass grafting
CCTA	coronary computed tomography angiography
COURAGE	Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
CTO	chronic total occlusion
CT-RECTOR	Computed Tomography Registry of Chronic Total Occlusion Revascularization
CTS-C-CTOPCI	Effect of Preoperative Coronary CT for Planning of Percutaneous Coronary Intervention for Complex Chronic Total Occlusion
DECISION-CTO	Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion
Ischemia CTO	International Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy of Chronic Total Coronary Occlusions with Myocardial Ischemia
ISCHEMIA	International Study of Comparative Health Effectiveness with Medical and Invasive Approaches
IVUS	intravascular ultrasound
KCCT	Korean Multicenter CTO CT Registry
NASA	Native Coronary Artery Instead of Saphenous Vein Graft Intervention for Treatment of Significant Saphenous Vein Graft Lesions Registry
OPEN-CTO	Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures
ORBITA CTO Pilot	Placebo-Controlled Trial of Chronic Total Occlusion Percutaneous Coronary Intervention for the Relief of Stable Angina
PCI	percutaneous coronary intervention
PROCTOR	Percutaneous Coronary Intervention of Native Coronary Artery Versus Venous Bypass Graft in Patients With Prior CABG
PROGRESS-CTO	Prospective Global Registry of Chronic Total Occlusion Interventions
RCT	randomized controlled trial
RENOVATE-COMPLEX-PCI	Randomized Controlled Trial of Intravascular Imaging Guidance Versus Angiography-Guidance on Clinical Outcomes After Complex Percutaneous Coronary Intervention
STAR	Subintimal Tracking and Reentry
SVG	saphenous vein graft

WHY PERFORM CTO PCI?

CTO PCI is a tool that can help achieve coronary revascularization. CTO PCI should be considered when the potential benefits outweigh the risks (Figure 2).[11,12] The key benefit of CTO PCI is to improve patient symptoms.[2] Although retrospective studies suggest that successful CTO PCI may also improve the incidence of death or myocardial infarction,[9] this remains unproven in prospective studies. This is consistent with findings from mid-term studies in mainly non-CTO stable coronary artery disease, such as the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) and the ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) trials in all-comers. It is also likely related to the lower baseline risk of patients enrolled in randomized-controlled trials (RCTs) and the lack of long-term follow-up.[13] CTO PCI carries risks for both acute (coronary perforation, acute vessel closure, side branch and periprocedural myocardial infarction, equipment loss/entrapment) and long-term (ie, stent thrombosis and in-stent restenosis) complications.

The EuroCTO[14] and 2 smaller single-center unblinded RCTs (Figure 3) showed a symptomatic benefits with CTO PCI without an increase in complications.[15,16] The larger DECISION-CTO trial (Drug-Eluting Stent Implantation Versus Optimal Medical Treatment in Patients With Chronic Total Occlusion) did not show symptom improvement but had multiple limitations, such as low power due to premature termination of enrollment, inclusion of patients undergoing PCI on non-CTO lesions in both arms and 20% crossover from the medical therapy arm to CTO PCI immediately after randomization.[17] This is why many CTO operators disagree with the downgrade of the indication for CTO PCI in the ACC/AHA guidelines (from IIA to IIb).[18] This contrasts with the European guidelines, which provide a level IIA recommendation for CTO PCI to improve symptoms.[19]

Table. 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, structured angiographic review should be performed in every case
3	Use of a microcatheter is essential for guidewire support
4	There are 4 CTO crossing strategies: antegrade wire escalation, antegrade dissection/reentry, retrograde wire escalation, and retrograde dissection/reentry
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

CTO indicates chronic total occlusion; and PCI, percutaneous coronary intervention.

Reproduced with permission from Brilakis et al[2].

Evidence-based medicine involves integrating the highest level of evidence into decision-making and guidelines and does not limit our evidence to RCTs, especially when RCTs may not enroll the full clinical spectrum of patients with CTO. A recent study comparing patients with CTO PCI enrolled in randomized trials versus real-world registries showed significant differences in anatomic and clinical features: patients in registries were much sicker, suggesting preferential enrollment of lower-risk and less symptomatic patients in RCTs.[13] On the other hand, multiple observational studies have shown lower long-term mortality following successful CTO PCI (48% lower in a recent meta-analysis).[9] The 10-year follow-up of the Canadian CTO registry showed higher survival associated with PCI or coronary artery bypass grafting (CABG) history in patients with CTOs, but only when the CTO was revascularized. Patients who underwent PCI only for non-CTO lesions or CABG without grafting of the CTO vessel had similar survival compared with patients managed medically.[20] However, it is a daunting task to determine definitively if CTO PCI can reduce mortality. To power a study to detect a 30% reduction in mortality with CTO revascularization compared with medical therapy assuming a baseline mortality of 3.6% as in the DECISION-CTO trial, 8000 patients would be needed, which is impractical. The multicenter DECISION CTO trial was stopped early before completing a 1200-patient planned sample size after 6 years of recruitment. To reduce the sample size, investigators often need to combine mortality with less important outcomes, such as hospitalization or outcomes that are unlikely to be affected by CTO PCI (eg, strokes), which may bias toward the null hypothesis.

Several ongoing studies could help address this controversy. The ORBITA CTO Pilot (Placebo-Controlled Trial of Chronic Total Occlusion Percutaneous Coronary Intervention for the Relief of Stable Angina; REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT05142215)[21] and the Ischemia CTO (International Randomized Trial on the Effect of Revascularization or Optimal Medical Therapy of Chronic Total Coronary Occlusions with Myocardial Ischemia; REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03563417, symptomatic arm)[22] will help assess the true effect of CTO on symptoms and harder outcomes. However, the impact of CTO PCI on mortality is unlikely to ever be tested in a large enough powered trial. As a result, the best available data may remain registry data. Clinical decision-making should take these data into account in addition to the data from underpowered RCTs that recruited lower-risk patients due to the impracticality of randomizing symptomatic patients.

Post-CABG patients with failing grafts are often referred for PCI of the corresponding native artery CTOs instead of undergoing PCI of the failing graft, usually a saphenous vein graft (SVG), especially in the context of an acute coronary syndrome, recurrent in-stent restenosis, or severely degenerated SVG.[23] These patients are under-represented in trials. The ongoing PROCTOR (Percutaneous Coronary Intervention of Native Coronary Artery Versus Venous Bypass Graft in Patients With Prior CABG; REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03805048) is comparing native vessel PCI with SVG PCI in patients with a dysfunctional venous bypass graft with a clinical indication for revascularization. The NASA (Native Coronary Artery Instead of Saphenous Vein Graft Intervention for Treatment of Significant Saphenous Vein Graft Lesions Registry; REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT05187351) is also evaluating the outcomes of native coronary artery PCI in patients presenting with severe SVG lesions.

PLANNING CTO PCI

Once the decision to perform CTO PCI is made, planning begins. The key question is how to successfully complete the procedure in the most safe and efficient way. Planning includes multiple components, such as selecting access sites and equipment (guide catheters, microcatheters, wires, intravascular imaging, lesion preparation devices, hemodynamic support) and choosing procedural strategies.[24] Planning is based on the patient's clinical characteristics and the angiogram (both the invasive coronary angiogram and increasingly coronary computed tomography angiography (CCTA) as described in the section "Coronary CT Angiography".

Dual injection, that is, contrast administration in both the CTO and the donor vessel that provides collaterals, remains critical for nearly all CTO PCIs.[2] A detailed review of the angiogram (focusing on 4 characteristics: proximal cap, occluded segment, distal vessel, and collaterals) helps select the optimal CTO crossing strategy, as

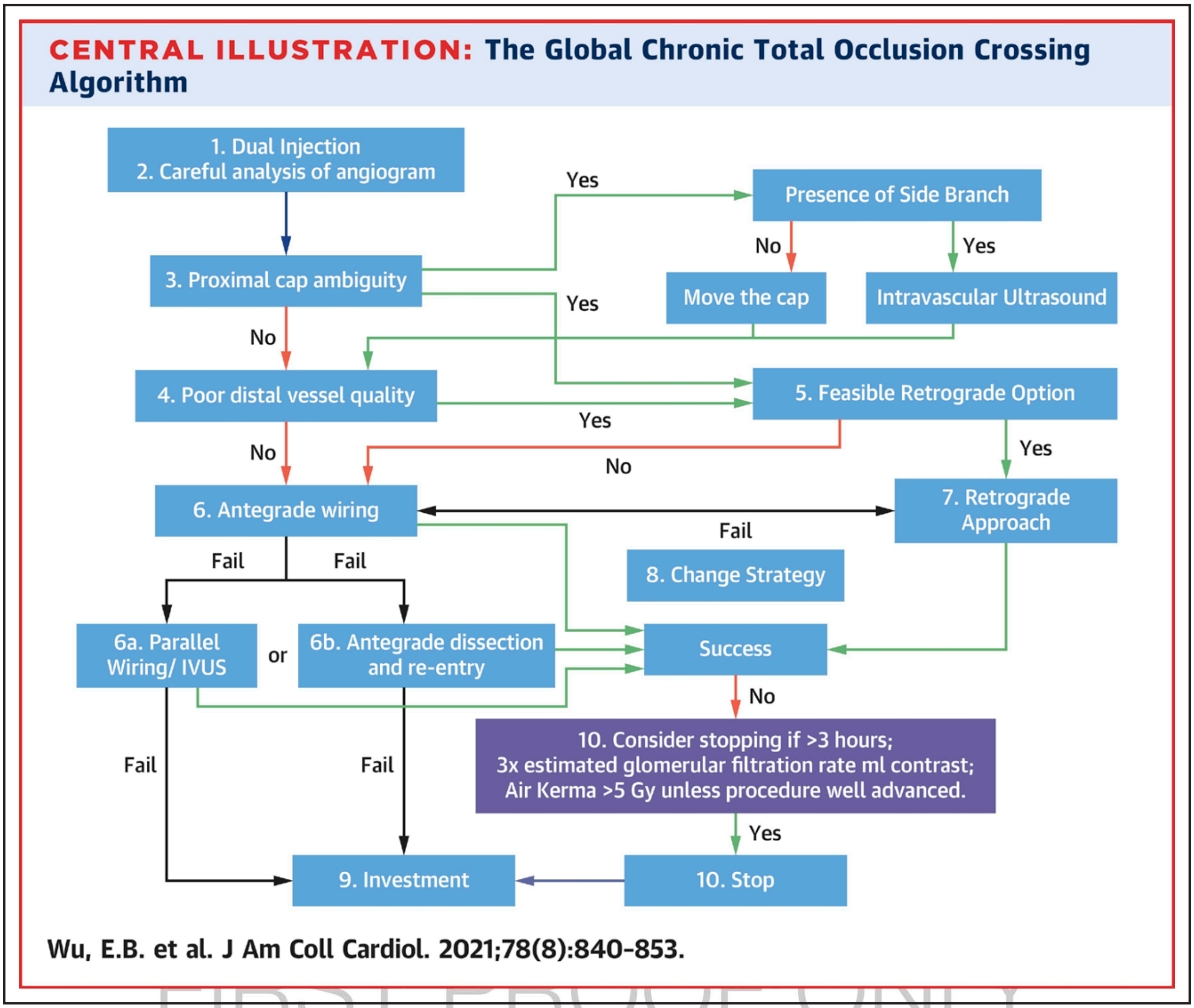

Figure 1. The global chronic total occlusion (CTO) crossing algorithm.
Gy indicates gray; and IVUS, intravascular ultrasound. Reproduced with permission from Wu et al[4].

outlined by the global CTO crossing algorithm.[4] Artificial intelligence-based analysis of the angiogram is an evolving tool and can improve the prediction of antegrade wiring success.[25] Several angiographic (such as the J-CTO, PROGRESS-CTO [Prospective Global Registry of Chronic Total Occlusion Interventions], and CASTLE: CABG age [≥70 years], stump anatomy [blunt or invisible], tortuosity degree [severe or unseen], length of occlusion [≥20 mm], and extent of calcification [severe]) and computed tomography angiography (such as the CT-RECTOR [Computed Tomography Registry of Chronic Total Occlusion Revascularization] and KCCT [Korean Multicenter CTO CT Registry]) scores have been developed to assist with prediction of guidewire crossing time and technical success, and can facilitate procedural planning.[26] There are also scores to assess the risk of complications, such as the PROGRESS-CTO MACE score.

Using a single injection decreases the likelihood of success and increases the risk of complications. It should be reserved for operators highly experienced in a minimalistic approach and possibly for rarer cases of ipsilateral collaterals without evident contralateral collaterals.[27] Access site selection depends on the patient's vascular anatomy and operator preference: radial-femoral access is most commonly used, followed by bifemoral and biradial access.[28,29] Optimal vascular access techniques, including the use of fluoroscopy, ultrasound,[30] micropuncture tools, femoral angiography, and vascular closure devices are essential.

CORONARY CT ANGIOGRAPHY

CCTA has been used for planning CTO PCI for several years, but as a result of the ISCHEMIA trial and other studies, it is increasingly recognized as the preferred noninvasive anatomic modality to evaluate patients with suspected or established coronary artery disease. CCTA can be specifically ordered for the preprocedural planning of

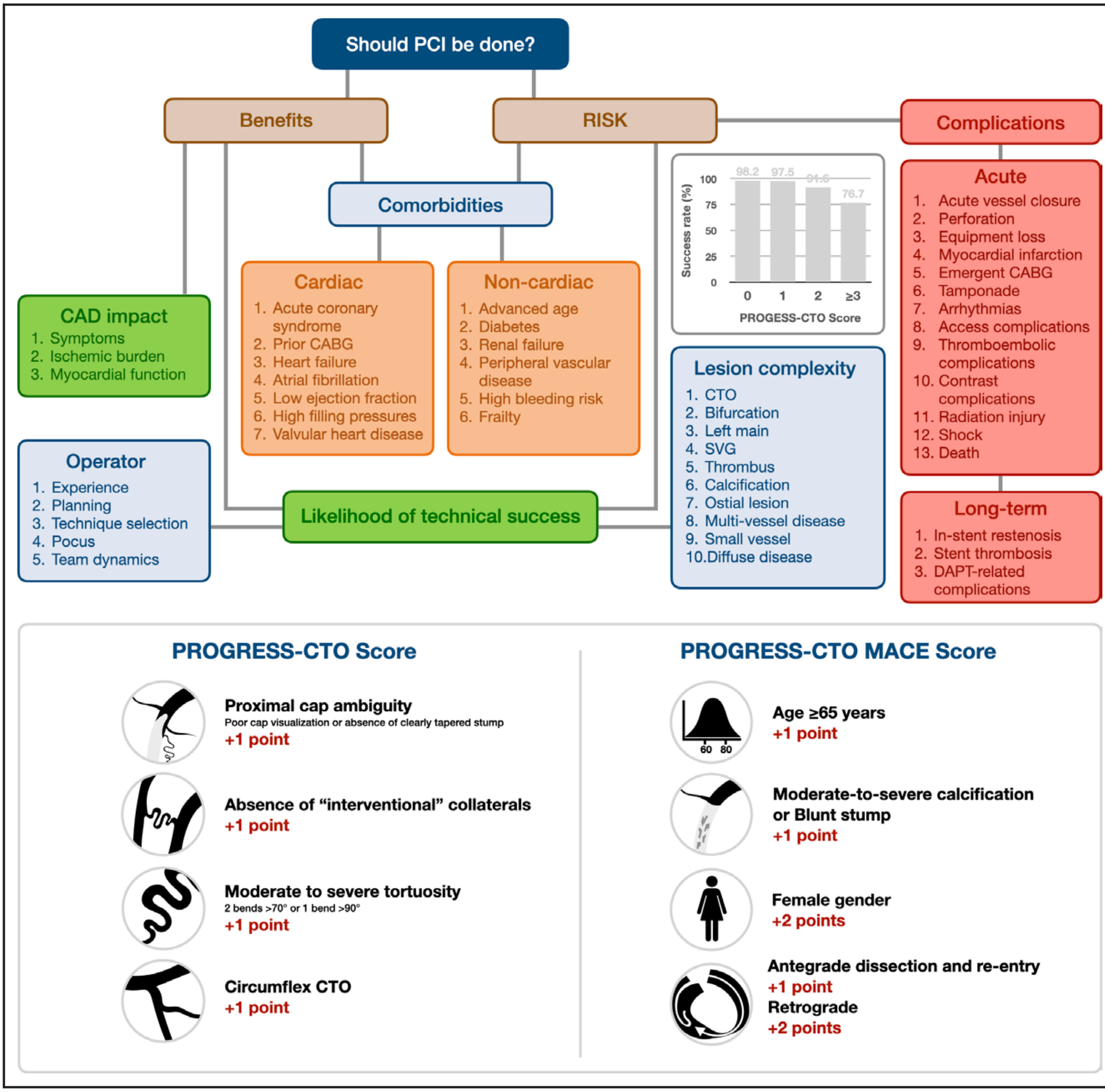

Figure 2. Assessing the risks and benefits of chronic total occlusion (CTO) percutaneous coronary intervention (PCI).
CABG indicates coronary artery bypass graft surgery; CAD, coronary artery disease; DAPT, dual antiplatelet therapy; and SVG, saphenous vein graft.

CTO PCI, but patients are also increasingly referred for CTO PCI based on CCTA alone without undergoing an invasive coronary angiogram. CCTA can streamline care and facilitate referrals to specialized centers for CTO PCI.

There are multiple CCTA-based risk scores[31–33] that can be used to facilitate shared-decision-making and preprocedural planning (Figure 4), and these seem to be superior to angiography-based scores.[26] The Role of CT Scan for the Successful Recanalization of CT-CTO randomized trial showed that preprocedural CCTA was associated with a higher success rate, especially in patients with more complex CTOs.[34] However, the implementation of CCTA planning remains limited in CTO PCI, largely due to the limited expertise of interventional cardiologists in CCTA analysis, as well as institutional and systemic workflow constraints. Communication with CT reading experts can be extremely useful but novel artificial intelligence-based software has recently become available, greatly simplifying CCTA review. CCTA can assist in selecting the appropriate guide catheters by recommending AL guide catheters for anterior origin of the right coronary artery or by matching the size of the left guide to that of the aorta. It can also provide the optimal angiographic angles to visualize CTO segments. CCTA can help clarify proximal cap ambiguity[35] and vessel course, accurately measure occlusion length and plaque composition, assess for myocardial bridges[36] and help with crossing strategy selection. For example, when

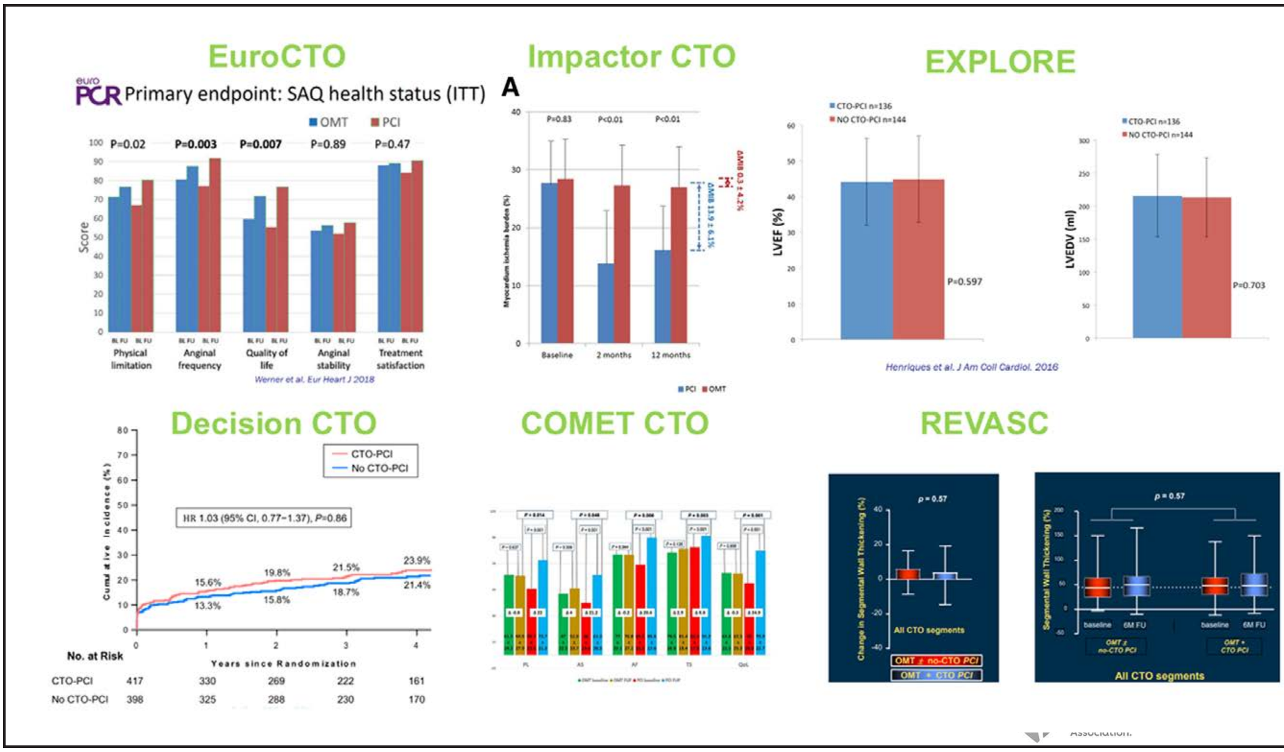

Figure 3. Summary of the randomized trials of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) vs no CTO PCI.

COMET CTO indicates Randomized-Controlled Comparison of Optimal Medical Therapy with Percutaneous Recanalization of Chronic Total Occlusion; CTO, chronic total occlusion; DECISION-CTO, Drug-Eluting Stent Implantation vs Optimal Medical Treatment in Patients With Chronic Total Occlusion; EXPLORE, Evaluating Xience and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Segment Elevation Myocardial Infarction; IMPACTOR-CTO, Impact on Inducible Myocardial Ischemia of Percutaneous Coronary Intervention vs Optimal Medical Therapy in Patients with Right Coronary Artery Chronic Total Occlusion; ITT, intention to treat; LVEF, left ventricular ejection fraction; REVASC, Recovery of Left Ventricular Function After Stent Implantation in Chronic Total Occlusion of Coronary Arteries; and SAQ, Seattle Angina Questionnaire.

calcium is present in the entire lumen and vessel wall (a full moon appearance), the procedural risk increases and extraplaque crossing techniques are needed, along with advanced plaque modification.[5] CCTA can help identify the plaque-free or calcium-free side for reentry procedures[37] and guide CTO wire selection. CCTA can help with stent size and length selection but is limited in collateral assessment due to their small size and relatively low resolution of CCTA.

Coregistration of CCTA with coronary angiography has been successfully used to guide CTO crossing,[38] but its use remains limited due to difficulties integrating CCTA data sets onto real-time fluoroscopy images. The ongoing P4 trial, which randomizes patients to intravascular ultrasound (IVUS) or CCTA-guided PCI, includes patients undergoing CTO PCI. In those randomized to CCTA, there is CCTA coregistration with a 3-dimensional model displaying coronary anatomy, vessel course, plaque, and calcification in synchronization with the C-arm.

CCTA findings are more accurate in predicting the likelihood of CTO PCI success and antegrade wiring than invasive angiography, and there are several CT-based scores.[26] Artificial intelligence-based CCTA analysis was recently shown to provide an outstanding prediction of procedural success and guidewire crossing within 30 minutes[39] and is likely to be increasingly used in the future.

There are several ongoing studies on the use of CCTA in CTO PCI, such as the CTS-C-CTOPCI (Effect of Preoperative Coronary CT for Planning of Percutaneous Coronary Intervention for Complex Chronic Total Occlusion; REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04549896).

MONITORING

Continual monitoring of the patient is critical in every CTO PCI for the prevention and early diagnosis of complications, especially perforations. The activated clotting time should be frequently monitored (usually every 30 minutes), aiming for an activated clotting time of >300 for antegrade and >350 seconds for retrograde procedures.[40] Immediate access to cardiac ultrasound is essential in the setting of hypotension to assess for hemodynamically significant effusions. In patients with congestive heart failure or low left ventricular ejection fraction, the use of right-heart catheterization to monitor

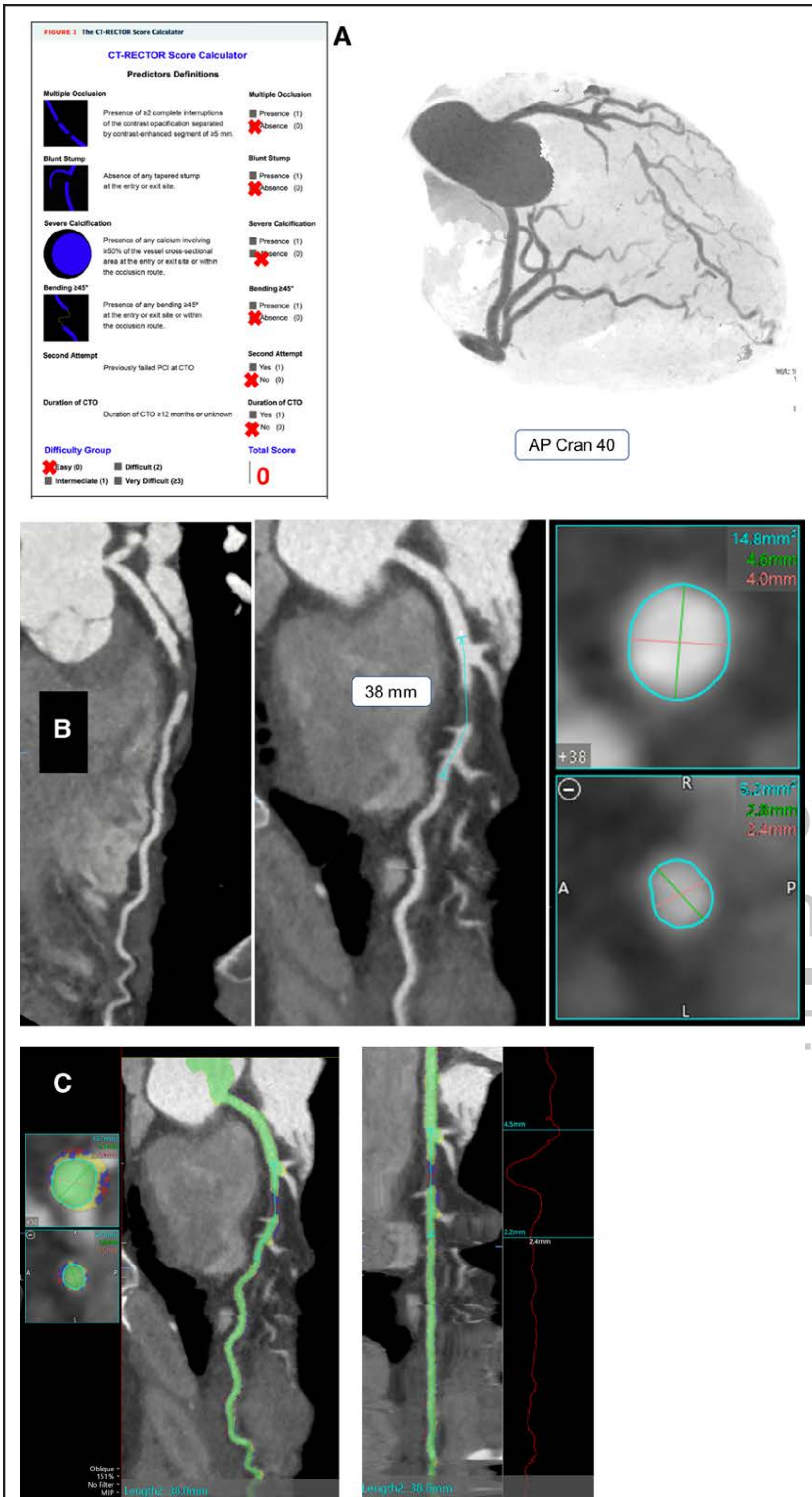

Figure 4. Example of coronary computed angiography for guiding CTO PCI.
A, Maximum intensity projection of a coronary computed tomography angiography showing a mid-left anterior descending artery chronic total occlusion with a low CT-RECTOR score. **B** and **C**, Multiplanar reconstruction allowing estimation of stent length and diameter. There is no significant calcification. CT-RECTOR indicates Computed Tomography Registry of Chronic Total Occlusion Revascularization; and KCCT, Korean Multicenter CTO CT Registry.

wedge and pulmonary artery pressures can help assess the tolerance of the procedure and determine the need for hemodynamic support. Finally, a team approach with all catheterization laboratory staff involved in assessing the patient's comfort and tolerance to the procedure is key to avoiding complications.

CROSSING THE CTO

Inability to cross the occlusion with a guidewire remains the most common cause of CTO PCI failure. CTO crossing can occur in both the antegrade and retrograde directions, either intraplaque (within the prior location of the vessel lumen) or extraplaque (within the vessel wall). The ability to implement the retrograde approach significantly increases success rates, especially in complex CTOs, but also carries an increased risk of complications[41] likely at least in part due to higher disease complexity.[42]

ANTEGRADE CROSSING TECHNIQUES

Antegrade wiring is the most commonly used CTO PCI technique. Soft, tapered-tip, polymer-jacketed wires are initially used in most cases followed by escalation to stiffer-tip guidewires and de-escalation to softer wires as needed. Newer guidewires and microcatheters[43] have improved the success rate of antegrade wiring, but advancement of the wires in the extraplaque space remains common, necessitating reentry. IVUS guidance can facilitate antegrade wiring by clarifying proximal cap ambiguity or determining wire position and facilitating reentry. Antegrade dissection is typically performed using polymer-jacketed guidewires, with the Asahi Intecc Gladius Mongo (Asahi Intecc, Aichi, Japan—called Gladius MG [microgap] outside the United States) being a specifically designed wire for traveling knuckling.[43,44] Other polymer-jacketed wires commonly used for knuckling are the Fielder XT (Asahi Intecc) that forms tight knuckles and the Pilot 200 (Abbott Vascular, Santa Clara, California) that is stiffer and forms larger knuckles. Advancing knuckled wires is generally safe unless the wire enters a side branch or exits a distal small branch after reentry. Hence, orthogonal X-ray projections are essential to confirm the wire's course before advancing the microcatheter. The Stingray balloon (Boston Scientific, Natick, MA) has traditionally been used for reentry but its use has been decreasing, in part, due to high cost, limited access, steep learning curve, moderate success rates, and sometimes difficult delivery.[45] The ReCross (IMDS, the Netherlands) is the only dual-lumen microcatheter on the market with 2 over-the-wire lumens and has been used in some cases for reentry. It also allows aspiration of hematoma through the lumen not used for reentry, thus decompressing the extraplaque space and potentially facilitating reentry.[46] Antegrade fenestration and reentry use balloon inflations at the proximal cap, while advancing a polymer-jacketed guidewire into the distal true lumen. The Subintimal Antegrade Fenestration Reentry technique uses contrast injection to create a dissection followed by multiple antegrade balloon inflations to create a fenestration through which a polymer-jacketed wire is advanced.[47] A novel imaging-based catheter has been developed to facilitate CTO reentry but is not currently clinically available.[48] The upcoming Triumph catheter (Teleflex, Wayne, PA) is another specialized ADR catheter with 6 wire exit ports for reentry and also allows aspiration for decreasing the size of the extraplaque hematoma. Tip-detection ADR is a newer, technically demanding strategy that uses IVUS to direct the guidewire (such as the highly penetrating Conquest Pro 12 Sharpened Tip, Asahi Intecc) into reentering the true lumen.[49,50] Hydrodynamic contrast recanalization is another novel antegrade crossing technique that combines contrast microinjections and polymer-jacketed wires for antegrade CTO crossing.[51]

RETROGRADE CROSSING TECHNIQUES

The retrograde approach has been and continues to be an excellent solution for complex CTOs, especially when antegrade crossing fails.[41] The use of advanced guidewires, such as the Suoh 03 (Asahi Intecc, preferred for epicardial collaterals) and Sion and Sion black (Asahi Intecc), as well as microcatheters, such as the Turnpike LP (Teleflex), and Corsair Pro XS and Caravel (Asahi Intecc), enables crossing of complex collaterals. The use of epicardial collaterals is more risky and has been decreasing,[52] while the use of investment procedures employing STAR (Subintimal Tracking and Reentry) or subintimal plaque modification has been increasing (see section "Modification Procedures").[45]

Reverse controlled antegrade and retrograde tracking is the most common retrograde crossing technique and can be facilitated by use of an antegrade guide extension (guide extension reverse controlled antegrade and retrograde tracking) and IVUS. Sometimes, connecting the antegrade and retrograde space can be difficult, requiring IVUS-guided sizing of the antegrade balloon, directed puncture with penetrating wires toward an antegrade balloon, and other innovative techniques, such as intracoronary snaring of the retrograde guidewire.[53]

After retrograde CTO crossing, guidewire externalization of a long dedicated guidewire (≥330 cm) is performed in most (≈90%) cases. Alternative strategies to externalization are increasingly being used,[54] especially after retrograde crossing via epicardial collaterals, to minimize the risk of collateral injury.[55] In the tip-in technique, an antegrade microcatheter is advanced over the retrograde guidewire inside the antegrade guide catheter. In the rendezvous technique, an antegrade wire is advanced inside the retrograde microcatheter, usually within the CTO body. Finally, converting to an antegrade system after externalization with a single-lumen or dual-lumen microcatheter delivered on the externalized wire is a commonly used technique to reduce the dwell time through any collateral and convert the retrograde to an exclusive antegrade system.

Whether to occlude a patent bypass graft after recanalization of the native CTO remains controversial. A recent study showed a higher risk of CTO failure after 1 year in the patent versus occluded SVG group.[56] The decision about SVG closure is usually made based on the degree of residual competitive flow from the SVG after successful recanalization of the native CTO.

COMPLEX SUBGROUPS

Some types of CTOs can be more challenging to recanalize:

- CTOs in prior CABG patients: These patients often have more complex anatomy, frequently with severe calcification, but they also often have additional options for retrograde crossing through bypass grafts.[57] Coronary perforation can be a life-threatening complication in such patients, as it can lead to loculated hematomas that cannot be drained percutaneously.[58,59]
- Flush aorto-ostial CTOs: Such CTOs usually require a primary retrograde approach, but reentry into the aorta can be challenging.[60] Electrocautery-assisted reentry has been successfully used in such cases.[61] Another option is the Power Flush[62] (forceful injection of contrast dye directly through the guiding catheter positioned against the aortic wall in correspondence to the coronary ostium location) and the original controlled antegrade and retrograde tracking technique.[63]
- CTOs with bifurcations at the proximal and distal cap or within the occluded segment: Recanalization of all major side branches is desired in such patients and can often be achieved using IVUS, dual-lumen microcatheters, the retrograde approach, and STAR (as a bailout).[63–65] CTOs of the left main coronary artery are associated with more calcification and anatomic ambiguity, in addition to the potential for major vessel occlusion (left anterior descending artery or circumflex).
- CTOs in patients with left ventricular dysfunction and poor hemodynamics: CTO PCI should be deferred in patients with hemodynamic decompensation until their hemodynamics are optimized. Urgent hemodynamic support was used in 2.2% of CTO PCIs in the PROGRESS-CTO registry and was more likely to be needed in patients treated with a retrograde crossing strategy, lower left ventricular ejection fraction, and longer lesion length.[66]
- Heavily calcified CTOs: Moderate/severe calcification is present in nearly half of CTOs and requires more frequent use of the retrograde approach and advanced plaque modification techniques. It is also associated with lower technical and procedural success, and higher major adverse cardiovascular events.[67]

MODIFICATION PROCEDURES

Staged procedures may be required to recanalize a CTO and may benefit from modifying the CTO during the initial unsuccessful procedure. CTO-ARC defines CTO modification (sometimes also called investment procedure as intentional balloon dilatation [diameter ≥2.0 mm]) of the entire CTO, including the proximal and distal caps and the CTO body.[8]

CTO modification without distal true lumen reentry is called subintimal plaque modification. CTO modification after distal wire reentry into the true lumen is called modified STAR with balloon angioplasty only (without stent implantation), followed by repeat angiography and PCI 2 to 3 months later. This is currently the most used antegrade extraplaque crossing technique in the United States.[45] IVUS can facilitate STAR.[68] Occasionally, upfront stenting is performed after crossing with STAR if there is adequate preservation of key side branches and acceptable anticipated stent length.

The optimal timing of repeat angiography (2 versus 4 months) is currently being examined in the STAR trial (REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT05089864).[69] The INVEST-CTO study (REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT04774913) is a prospective, single-arm, international, multicenter study evaluating the effectiveness and safety of a planned CTO modification procedure, with a subsequent completion CTO PCI (at 8–12 weeks), in anatomically high-risk CTOs.

INTRAVASCULAR IMAGING

Intravascular imaging is essential for complex PCI, including CTO PCI. IVUS is preferentially used to avoid contrast injection that is needed for OCT and can extend dissection planes. Either IVUS or OCT can be used for stent optimization after deployment. There is ample evidence on the benefit of IVUS for CTO PCI[70]: most recently, the RENOVATE-COMPLEX-PCI trial (Randomized-Controlled Trial of Intravascular Imaging Guidance Versus Angiography Guidance on Clinical Outcomes After Complex Percutaneous Coronary Intervention) demonstrated that the superiority of intravascular imaging over angiography guidance alone was greater in patients undergoing CTO PCI than in all-comers.[71] Imaging is used for CTO crossing (eg, to resolve proximal cap ambiguity), lesion preparation, stent optimization, and confirmation that an optimal result has been achieved.

LESION PREPARATION

Lesion preparation is critical for achieving adequate stent expansion. Due to ease of use and safety, intravascular lithotripsy recently surpassed coronary atherectomy as the most commonly used technique for calcium modification in CTO PCI in a large registry.[72] Intravascular lithotripsy can also facilitate entry into the extraplaque space.[73,74] Atherectomy remains, however, essential, especially when equipment delivery to the lesion is challenging but likely carries increased risk when performed in the extraplaque space.[75] Specific algorithms have been developed for approaching balloon-uncrossable[76,77] and balloon-undilatable lesions.

Landing a stent in a myocardial bridge after CTO PCI carries a high risk for subsequent adverse events and should be avoided.[36] Whether drug-coated balloons might obviate or reduce the need for extensive stenting during CTO PCI is under investigation.

EFFICIENCY

The mean CTO procedure time in the Progress-CTO registry is ≈2 hours; most of the time is used for stent deployment and stent optimization.[10] The efficiency of CTO PCI has significantly improved over time, likely due to the wide adoption of the hybrid, the global and other CTO crossing algorithms, improvements in equipment and techniques, and extensive training and communication among operators. Incorporating artificial intelligence-based tools[25,33,78] could further improve the efficiency of CTO PCI.

Same-day discharge is increasingly being used in CTO PCI. In a large single-center registry from the Netherlands, 62% of cases were discharged the same day without increased complications.[79]

SUCCESS

The success of CTO PCI is currently high (85–90%) when performed by experienced operators across multiple regions of the world.[3,80–82] It is significantly lower, however, in national or regional registries where CTO PCI is mainly performed by less skilled operators.[1] To ensure that CTO PCI is performed with the highest chance of success and safety, further training of existing and new operators is needed, as well as establishing referral pathways. The use of simulators can facilitate education, whereas remote proctoring[83] can allow both training and live case support.

COMPLICATIONS

CTO PCI is associated with a higher risk of complications, especially perforation, which remains the most feared complication of CTO PCI.[58] Availability of perforation management equipment (covered stents and coils) and familiarity with their use is required in all catheterization laboratories.[84] Inflation of a 1:1 sized balloon proximal to or at the site of the perforation to stop bleeding into the pericardium is the first step in managing a perforation.[85] Implantation of a covered stent is usually performed in large vessel perforation, and coil or fat embolization in distal vessel perforations. In the OPEN-CTO (Outcomes, Patient Health Status, and Efficiency in Chronic Total Occlusion Hybrid Procedures) registry, the incidence of perforation was 8.9%, and 55.1% of perforations were due to antegrade wiring.[86] Perforation of epicardial collaterals can cause tamponade and often requires embolization from both sides of the perforated vessel.

The recent introduction of a perfusion balloon (Ringer, Teleflex) allows prolonged balloon inflation and distal equipment delivery without causing severe ischemia.[87] Another less commonly used way to treat coronary perforations in selected patients is to create a dissection plane around the perforated area that can seal the perforation.[88,89] Implementation of this technique requires operator expertise in entering and managing the extraplaque space.

Donor vessel injury or embolization can be a life-threatening complication of CTO PCI as it can lead to profound ischemia and rapid hemodynamic deterioration.[90] A dedicated safety wire should be inserted in all donor vessels to expedite the treatment of donor vessel injury.[91] Moreover, the Wire in Aorta for Localization and Protection of the Ostium technique where an additional wire is placed into the sinus, can be used in several scenarios, especially after externalization, to avoid deep seating of a donor guide catheter.[92] Donor vessel angiography should be immediately performed in case of hemodynamic deterioration or ischemic changes and also after completion of CTO PCI. Side branch occlusion as well as collateral compromise can also lead to periprocedural myocardial infarction.

Equipment loss or entrapment is the third major category of CTO PCI complications and detailed algorithmic approaches have been published to tackle this challenge.[93,94] Guidewire entrapment can sometimes be treated by rotational atherectomy to cut the wire, followed by stenting over the retained fragment.[95] Broken wire fragments can sometimes be retrieved with rapid twisting of a knuckled polymer-jacketed guidewire (knuckle twister technique[96]), but it is often easier to cover them with a stent.

A global consensus document on managing CTO PCI complications was published in 2024.[97]

PHYSICIAN WELL-BEING

CTO PCI can be stressful, as suggested by a larger increase in the heart rate and blood pressure of the operator as compared with non-CTO PCI in a multicenter study.[98] Implementation of wellness-enhancing activities, such as exercise and meditation, as well as mental health counseling if needed, might help mitigate some of these adverse effects. Prolonged procedures, such as CTO PCI, may increase the risk of spine and other orthopedic injuries. Moreover, there has been a plateau in the reduction of patient and operator radiation dose during CTO PCI,[99] which could potentially be overcome by the implementation of novel radiation protection systems, such as the IC Rampart, Zero Gravity, tProtego, and EggNest.

Development of a successful CTO PCI program requires institutional support not only for ensuring that adequate resources are available but also to avoid penalizing CTO PCI operators in terms of productivity, physician reimbursement for CTO PCI remains low given the time and expertise required. Future improvements in physician reimbursement could facilitate the recruitment and training of additional CTO PCI operators.

Several podcasts (Journey to Better, Alex & Friends, Sensei) have recently been created to inspire and support operators learning and performing CTO PCI. Moreover, several social media platforms (YouTube, X, LinkedIn) allow the rapid dissemination of novel techniques and sharing of information that can enhance the operators' knowledge and skills.

CONCLUSIONS

CTO PCI is a vibrant and dynamic field that has transformed PCI, enabling the treatment of increasingly complex lesions. Further improvements remain possible through collaboration, the development of new equipment and techniques, and the training of the next generation of CTO and complex PCI operators.

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