Percutaneous recanalisation of chronic total occlusions: 2019 consensus document from the EuroCTO Club

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KEYWORDS

Abstract

Since its inception in December 2006, the EuroCTO Club has strived to provide the framework for state-of-the-art chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in Europe and nearby regions. Among its initiatives, the EuroCTO Club has published a set of recommendations regarding the technical aspects of CTO PCI, whose last edition dates to 2012. The EuroCTO Club consensus document discusses CTO PCI clinical indications, techniques and equipment use, as well as the qualifications of operators/centres. Given the considerable amount of progress made by this subspecialty in recent years, there is a need for an updated document that includes data from recent clinical trials and registries, information on novel devices and techniques, and an up-to-date revision on the training requirements to approach CTO PCI. The current updated consensus document of the EuroCTO Club reflects the expertise of European operators to promote the widespread application of state-of-the-art CTO PCI, not only in Europe but also across neighbouring communities.

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Abbreviations

ADR   antegrade dissection re-entry
AWE   antegrade wire escalation
CABG   coronary artery bypass grafting
CART   controlled antegrade retrograde tracking
CTO   chronic total occlusion
DAPT   dual antiplatelet therapy
DES   drug-eluting stent(s)
EES   everolimus-eluting stent(s)
IVUS   intravascular ultrasound
MDCT   multidetector computed tomography
OMT   optimal medical therapy
OTW   over-the-wire
PCI   percutaneous coronary intervention
SES   sirolimus-eluting stent(s)
STEMI   ST-elevation myocardial infarction
TIMI   Thrombolysis In Myocardial Infarction

Introduction

The EuroCTO Club was established in December 2006. The first two consensus documents on the recanalisation of chronic total occlusions (CTOs) were published in 2007 and 2012[1,2], respectively, to provide an overview of CTO-dedicated material and to try to set standards on clinical indications, techniques and equipment use, and the qualifications of operators/centres. Since 2012, there have been considerable changes in practice, in parallel with the publication of a plethora of novel data, dramatically changing the landscape of CTO percutaneous coronary intervention (PCI).

For this reason, the EuroCTO Club has written this updated consensus document, reflecting the expertise of European operators to promote the widespread application of state-of-the-art CTO PCI in Europe and neighbouring communities.

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DEFINITION AND EPIDEMIOLOGY

Coronary CTO is defined as a 100% stenosis with Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow for more than three months[1,2]. Non-intralesional ipsilateral bridging collaterals may provide antegrade flow to the vessel beyond the occlusion and give a false impression of a functional incomplete occlusion. This should be distinguished from flow within the occluded segment by a careful frame-by-frame assessment in different angiographic projections.

Coronary CTOs are relatively common, observed in approximately 15-25% of patients with coronary artery disease undergoing coronary angiography[3-7]. The right coronary artery is the most common CTO vessel, representing about half of the CTO cases[5]. The CTO prevalence is much higher (~90%) among patients with prior coronary artery bypass grafting (CABG)[5], while a CTO is found in only one tenth of patients referred for ST-elevation myocardial infarction (STEMI)[8].

COLLATERAL CIRCULATION IN CTOs

The typical feature of a CTO is the presence of collaterals, found in ~90% of cases[5]. They have the capacity to preserve myocardial function but will not prevent ischaemia during exercise due to a limited capacity to increase blood flow[9]. The collateral supply provides a perfusion pressure in the range of 30-40 mmHg at the occluded territory, a pressure that leads to the functional reduction of distal vessel size, which then leads to the underestimation of the vessel dimensions during a recanalisation procedure[10]. The presence of collaterals does not predict viability, as they also develop in patients with prior myocardial infarction and large akinetic territories, i.e., viability still needs to be tested in well collateralised CTOs[11]. Moreover, the presence of a well-developed network of collaterals is not protective towards ischaemic insults, as even in such a patient population revascularisation might provide a survival benefit compared with medical therapy[12].

The angiographic assessment has been refined beyond the classic Rentrop classification by introduction of the grading of the collateral connection size[13], which is also helpful to select the appropriate guidewires and techniques for collateral crossing. A more detailed analysis of collateral supply led to the introduction of a collateral scoring system for the suitability for retrograde transcollateral interventions[14].

RATIONALE OF CTO REVASCULARISATION

Viable myocardium subtended by a CTO is generally ischaemic, regardless of the degree of collateralisation, as has been shown in fractional flow reserve (FFR) studies[15,16]. CTO recanalisation aims to improve myocardial perfusion of the corresponding ischaemic territory[17]. This in turn has beneficial effects at multiple levels (attendant on CTO success). First, successful CTO PCI relieves ischaemia[18,19], which has been shown to be associated with a decrease in severity and frequency of angina, as well as improved functional status and better quality of life[19,20]. Second, an untreated CTO is associated with incomplete revascularisation[21,22], which in turn has been associated with persistent left ventricular dysfunction at follow-up[23]. As such, CTO recanalisation allows complete revascularisation which might lead to improvement in left ventricular function[23]. Third, CTOs have an arrhythmic potential, as up to 3% of CTO patients present with malignant ventricular arrhythmias[5]. In a cohort of patients with implantable cardioverter-defibrillator, CTO subjects experienced a higher incidence of appropriate shocks for malignant ventricular arrhythmias, as compared to patients without CTO[24]. Moreover, ventricular arrhythmias can be observed even in the absence of myocardial scar, thus possibly being related to an ischaemic phenomenon[25].

Since there are only observational data[12] suggesting a mortality benefit for CTO recanalisation, consideration for intervention should be in order to improve symptoms and quality of life. Appropriate indication is thus important in CTO intervention, not least since this procedure is associated with increased costs, cath lab resource utilisation, and procedural risks, as compared with non-CTO PCI. CTO recanalisation is indicated in cases where a significant benefit is likely in terms of symptom relief, ischaemia reduction, and/or improvement in left ventricular function[17]. A baseline echocardiogram should be performed in

all CTO patients. In patients with normal wall motion or hypokinesia of the CTO territory, myocardial viability is assumed to be present, and CTO recanalisation should be undertaken in patients who remain symptomatic (with angina or dyspnoea on exertion) despite optimal medical therapy (OMT) (e.g., two anti-anginal medications), with the aim of achieving complete revascularisation. In asymptomatic patients, ischaemic burden evaluation is recommended, and CTO recanalisation is indicated if ischaemia is present in ≥10% of the left ventricular mass[18,26]. In case of akinesia/dyskinesia of the CTO territory, proof of viability with non-invasive imaging should be pursued, and CTO recanalisation is indicated only in patients with viable myocardium in the CTO territory, associated with symptoms or ischaemia[26]. While these are general consensus recommendations, patients should be judged for intervention on a case-by-case basis (e.g., in case of anti-anginal drug intolerance).

GUIDELINES, CTO PCI REGISTRIES, AND RANDOMISED TRIALS

Current guidelines recommend (class IIa B) that percutaneous revascularisation of CTOs should be considered in patients with angina resistant to medical therapy or with a large area of documented ischaemia in the territory of the occluded vessel[27].

One obstacle to a wider adoption of CTO recanalisation is the absence of robust evidence on the benefits of this treatment. Non-randomised comparative studies showed a beneficial effect of CTO recanalisation on symptoms, quality of life, and left ventricular function[12,28,29], while its impact on survival remains controversial[28-30]. However, this evidence is derived mostly from studies comparing patients with successful vs. unsuccessful CTO PCI and is therefore prone to important confounders.

Four randomised trials (RCTs) have now been published or presented. Each of these trials was modest in size and open-label in design. Definitive trials remain a scientific gap. The EXPLORE (Evaluating XIENCE and Left Ventricular Function in Percutaneous Coronary Intervention on Occlusions After ST-Elevation Myocardial Infarction) trial is based on the well-established observation of the disadvantage of a patient with a CTO when experiencing a STEMI ("double jeopardy")[31]. The trial randomised survivors of a STEMI within seven days to receive PCI or conservative management for a concomitant CTO in order to observe differences in left ventricular function at four months[31]. The trial did not show a difference, but it was hampered by a low success rate for CTO PCI (73%), a high crossover rate (23%), and the fact that those most likely to profit from CTO PCI were those who died early from shock.

The DECISION-CTO trial was presented at ACC 2017, and has not yet been published as an article. It randomised patients with a CTO to OMT vs. CTO PCI. Critical flaws in trial design include the fact that revascularisation of non-CTO lesions was allowed in both groups and observed in more than 70% of patients (thus diluting the real impact of CTO recanalisation on patient outcomes), extremely low enrolment even from high-volume centres (which

suggests a strong selection bias), an 18% crossover rate, and the inclusion of all-cause death and stroke in the primary endpoint (while PCI in all-comers in an elective setting has never shown benefits with regard to such endpoints). Not surprisingly, the trial did not find any difference in the primary endpoint.

In contrast, the EUROCTO trial[32], which also randomised CTO patients to OMT vs. CTO PCI, had all non-CTO lesions treated before randomisation, so the sole effect of a remaining CTO on symptoms could be evaluated (primary endpoint). The trial showed a superior effect of PCI on angina frequency and quality of life as compared with OMT, 12 months after randomisation[32]. Furthermore, physical limitation and functional angina class were improved. Of note, the success rate in that trial was 86.6%, thus in line with state-of-the-art CTO PCI worldwide[32].

Recently, the 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 randomly assigned patients with isolated CTO of the right coronary artery (RCA) to either PCI (n=32) or OMT (n=33)[33]. In the PCI group, Obedinskiy et al[33] demonstrated that the decrease in myocardial ischaemia burden at 12 months (primary endpoint) was significantly higher in comparison with the OMT group (13.9±6.1% vs. 0.3±4.2%; p<0.01). Similarly, functional status and quality of life only improved in the PCI group[33], confirming the findings of the EUROCTO trial in the setting of single-vessel disease CTO patients.
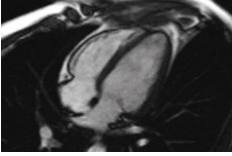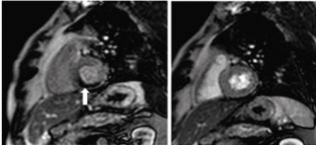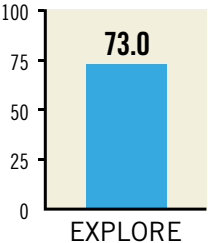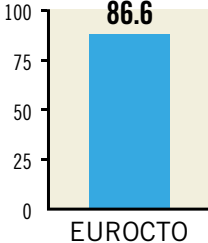
Figure 1 summarises the major results of the published randomised CTO trials.

Next to randomised trials, which always include a selected patient group, registries including all-comers are important for the assessment of trends in treatment. Currently, the longest-running and largest registry is the ERCTO registry, with more than 17,000 procedures recorded. Since its inception in 2008, this registry has witnessed an increase in lesion complexity, with a parallel increase in the use of the retrograde approach and in success rates[34].

Planning the CTO procedures
PREDICTIVE CTO SCORES

A key contributor to achieving success in CTO PCI is meticulous preparation. While the indication for CTO recanalisation should be clinical and not based on any score predicting the probability of technical success of the procedure, scoring models provide a quantitative measure of procedural difficulty and the probability of recanalisation success, which can help with clinical decision making. Furthermore, by providing more objective evaluation of anatomic and clinical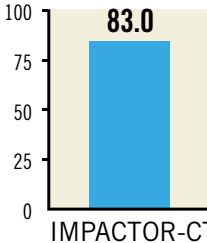 complexity, CTO scores enable better case selection according to operators' experience[35]. Finally, within the Heart Team, the decision to revascularise and the optimal strategy can be tailored to each CTO patient, taking into account the objective probability of achieving angiographic/clinical success with PCI.

	EXPLORE	EUROCTO	IMPACTOR-CTO
Location & design	Europe & Canada Multicentre RCT (14 centres)	Europe Multicentre RCT (28 centres)	Russia Single-centre RCT
N patients	304	407	72
Study population	Patients with STEMI treated with PCI with a non-infarct-related CTO	SCAD CTO patients with symptoms and/or ischaemia and viability	Patients with isolated dominant RCA CTO and stable angina
Primary endpoint	LVEF and LVEDV by CMR	QoL (SAQ, EQ-5D)	Stress / Rest ΔMIB by adenosine stress CMR
Follow-up period	4 months	1 year	1 year
Mean J-CTO score	2±1	1.82±1.07	1.92±0.86
Success rate	73.0 (EXPLORE)	86.6 (EUROCTO)	83.0 (IMPACTOR-CTO)
Positive/negative RCT	−	+	+

Major findings

	EXPLORE PCI / OMT	EUROCTO PCI / OMT	IMPACTOR-CTO PCI / OMT
MACE	No difference	No difference	No difference
QoL	N/A	Better	Better
Ischaemia reduction	N/A	N/A	Better
LVEF and LVEDV	No difference	N/A	N/A
	PCI of a CTO located in the LAD may improve LVEF and clinical outcome		

Figure 1. *Major findings of the published RCTs comparing PCI vs. OMT in CTO patients. ΔMIB: decrease in myocardial ischaemia burden; CMR: cardiac magnetic resonance; CTO: chronic total occlusion; EQ-5D: EuroQol 5 dimensions questionnaire; J-CTO: Japanese chronic total occlusion; LAD: left anterior descending; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; MACCE: major adverse cardiac and cerebrovascular events; MACE: major adverse cardiovascular events; MI: myocardial infarction; OMT: optimal medical therapy; PCI: percutaneous coronary intervention; QoL: quality of life; RCA: right coronary artery; RCT: randomised clinical trial; SAQ: Seattle Angina Questionnaire; STEMI: ST-segment elevation myocardial infarction*

The J-CTO (multicentre CTO registry in Japan) score is currently the most widely used score[36]. Independent predictors of failure (each given one point) that make up the J-CTO score include prior failed attempt, angiographic evidence of heavy calcification, bending ≥45° within the occluded segment, blunt proximal stump, and occlusion length >20 mm. CTO lesions are then graded as easy, intermediate, difficult, and very difficult (J-CTO scores of 0, 1, 2, and ≥3, respectively)[36]. While experienced operators can attempt even the toughest of cases with high success rates, operators early in their learning curve can select "simpler" cases (J-CTO score 0 or 1), referring those judged to be more difficult (J-CTO ≥2) to CTO-dedicated centres, or performing them with the guidance of a proctor[35].

Newer CTO scores highlight the variety of approaches to CTO PCI. The clinical and lesion-related (CL) score created based on primarily antegrade procedures may perform better for antegrade-only operators[37], whereas the ORA (ostial location, Rentrop grade <2, age ≥75 years) score and the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) score may be more suitable for predicting recanalisation success in retrograde or hybrid procedures[38,39].

MULTIDETECTOR COMPUTED TOMOGRAPHY (MDCT)

The importance of preprocedural multidetector computed tomography (MDCT) remains debatable. MDCT is more accurate than angiography for the definition of the CTO length, the presence of calcium, and the determination of vessel size and remodelling[40]. Recently, two MDCT-based scores (CT-RECTOR and KKCT) have been introduced[41,42]. Compared with the angiography-based J-CTO score, these MDCT scoring systems provide a more accurate non-invasive tool for predicting time-efficient guidewire crossing and final procedural success. MDCT is also indicated in case of long ambiguous CTOs, with poor path visualisation via collaterals and previously failed procedures[40]. In the cath lab, MDCT can also be of benefit for visualisation of the guidewire advancement and optimisation of viewing angles, taking advantage of co-registration. However, its availability is limited. Further studies are required to determine the added value of preprocedural MDCT in CTO PCI better.

FAILING CTO PCI – WHEN TO STOP

Although failure can be highly frustrating and demoralising, being able to accept it and learn and apply the lessons that failure provides is a critical step for the CTO operator. Indeed, the art of "knowing when to stop" is a key issue in CTO PCI to avoid major complications. Operators should consider stopping a CTO PCI attempt if the procedure time is >3 hours, if more than 4x the estimated glomerular filtration rate of contrast has been used or if the radiation dose is >5 Gy air kerma, unless recanalisation is already about to be completed (e.g., antegrade wire in the distal true lumen, or having crossed the retrograde collateral channel). In case of subintimal tracking with failure to re-enter the true lumen, planning a new attempt could be associated with better procedural outcome. Subintimal plaque modification by balloon angioplasty may alter the occlusion anatomy, favouring true-to-true wiring on a subsequent attempt[43]. In certain cases, the vessel can heal quite favourably and occlusion recanalisation can be observed. It is therefore not surprising that subintimal plaque modification can promote an improvement in quality of life and angina[44]. In case of no symptomatic improvement, the patient can be brought back and recanalisation re-attempted after six to eight weeks from the first attempt.

Although CTOs re-attempted after initial failure are associated with higher angiographic complexity, longer procedural duration and fluoroscopy time in comparison with first attempt CTO lesions, in experienced hands the success and complication rates were reported to be similar[45]. The number of times a procedure may be re-attempted is an individual question to be assessed carefully by the treating physician and the patient, and must take into consideration the severity of symptoms, likelihood of success, risk of complications, and the patient's wishes.

CTO materials and dedicated devices

GUIDEWIRES

Guidewire technology has largely evolved during the last decade and contributed to technique evolution and procedural efficiency. No single wire serves all lesions and all circumstances. Understanding the interaction of different kinds of guidewire (soft <1 gr, intermediate stiff 2-6 gr, stiff >9 gr) with different types of tissue (soft, hard and calcified) is of paramount importance. Soft (<1 gr) tapered polymeric composite core guidewires are suitable for soft tissue tracking (passive wire control). Intermediate stiffness (2-6 gr) tapered composite core guidewires are used for hard tissue tracking (active wire control), while very stiff (>9 gr) tapered guidewires are suitable for calcified tissue penetration[46].

In the early era of CTO PCI stiff wires, non-tapered (Miracle family) and tapered (Confianza family; both Asahi Intecc, Aichi, Japan), were predominantly used for lesion crossing. These wires were limited by incapacity to deflect and poor steerability in tortuous anatomy. In 2008, low tip stiffness (<1 gr) in combination with tapering, polymer and hydrophilic coating was introduced (Fielder™ XT; Asahi Intecc) and was proven to be very good for soft tissue tracking, offering a success rate of 30-40%, but it tended to over-deflect and was also not steerable in more complex anatomy. The advent of two technologies addressed the abovementioned limitations. The first one was the composite core technology, that became available in 2010-2011 (Asahi SION family), dramatically enhancing wire steerability and tip shape retention and which was also introduced in the low stiffness wires to improve their performance (Fielder XT-A/Fielder XT-R). The second one was based on the growing experience and understanding of CTOs over the years, that made it evident that penetration power and steerability can only be combined in intermediate stiffness wires. In 2013 a combination of composite core, tapering, polymeric and hydrophilic coating in

intermediate stiffness wires introduced the "deflection and rotation" concept that prevailed in modern CTO wiring (Gaia family; Asahi Intecc). The use of these wires will continue to increase in all anatomies except heavily calcified lesions, where very stiff wires are indispensable.

The milestones of CTO guidewire development are presented in **Figure 2** and an overview of the currently available CTO guidewires is presented in **Supplementary Table 1** [2,46].

MICROCATHETERS

In the current era of CTO PCI, guidewires should always be used with an over-the-wire (OTW) device (microcatheter or over-the-wire balloon) in order to ease torque in the tip response, preventing flexion, kinking, prolapse of the guidewire, and improving penetration ability. Microcatheters also allow reshaping or changing the guidewire without losing the distal position. Microcatheters are generally preferred to OTW balloons. Indeed, they are more flexible and track better. Moreover, they allow better understanding of distal tip position and have less tendency to kink than OTW balloons.

Table 1 illustrates the most commonly used microcatheters in CTO PCI.

Details concerning the use of several microcatheters are given in **Supplementary Appendix 1**.

DUAL LUMEN MICROCATHETERS

Dual lumen microcatheters consist of a rapid exchange delivery system in the distal segment associated with an OTW lumen along the catheter. A radiopaque marker band identifies the distal tip of each lumen; the distal band corresponds to the exit point of the rapid exchange segment and the proximal band marks the exit point of the OTW lumen.

The indications for dual lumen microcatheters in CTO PCI can be summarised as follows: a) parallel wire technique; b) wiring a CTO in the presence of a side branch at the proximal cap; c) wiring the distal true lumen without losing access to a side branch near the distal cap; d) antegrade wiring of the distal true lumen if the externalised retrograde guidewire crossed a collateral near the distal cap; e) wiring of difficult-to-access collaterals for the retrograde approach. Hence, such devices are useful to treat bifurcation lesions within the CTO body or located in close proximity to the proximal or distal cap, particularly when a long dissection is present and the second wire has to follow the same course as the first wire for optimal bifurcation treatment using either the one- or two-stent technique.

Figure 2. *Milestones in CTO guidewire technology. CTO: chronic total occlusion*

Table 1. An overview of microcatheters used in Europe.

Manufacturer	Catheter	Length	Distal shaft outer diameter
Asahi Intecc	Tornus	135 cm	2.1 and 2.6 Fr
	Corsair and Corsair Pro	135 cm, 150 cm	2.6 Fr
	Caravel	135 cm, 150 cm	1.9 Fr
Boston Scientific	Renegade™ 18	105 cm, 115 cm, 135 cm	2.5 Fr
IMDS	NHancer Pro X	135 cm, 155 cm	2.3 Fr
Roxwood (now BTG)	MicroCross® 14 and MicroCross® 14ES	155 cm	1.6 Fr
Terumo	Finecross®	130 cm, 150 cm	1.8 Fr
Teleflex	Venture®	145 cm (rapid exchange), 140 cm (over-the-wire)	2.2 Fr
	SuperCross™	130 cm, 150 cm Preformed tip angle (45˚, 90˚ or 120˚)	2.1 Fr
	Turnpike®	135 cm, 150 cm	2.6 Fr
	Turnpike® LP	135 cm, 150 cm	2.2 Fr
	Turnpike® Spiral	135 cm, 150 cm	3.1 Fr
	Turnpike® Gold	135 cm	3.2 Fr
Acrostak	M-CATH	135 cm	2.25 Fr
Merit Medical	SwiftNINJA	125 cm	2.4 Fr

Asahi Intecc, Aichi, Japan; Boston Scientific Corp., Marlborough, MA, USA; IMDS, Roden, the Netherlands; BTG, Bothell, WA, USA; Terumo Corp., Tokyo, Japan; Teleflex/Vascular Solutions, Minneapolis, MN, USA; Acrostak, Geneva, Switzerland; Merit Medical, Galway, Ireland

An overview of the currently available dual lumen microcatheters is presented in **Supplementary Table 2**.

SUPPORT CATHETERS AND GUIDE EXTENSION CATHETERS

An overview of the utility and use of currently available support catheters and guide extension catheters is presented in **Supplementary Appendix 2** and **Supplementary Table 3**.

Techniques for CTO recanalisation
ACCESS ROUTE – GUIDING CATHETER SELECTION, CONTRALATERAL INJECTION

For CTO recanalisation, it is mandatory to ensure an optimal guide catheter support with a large enough lumen to host devices in parallel, as well as two arterial sheaths for contralateral injections. Good ipsilateral collateralisation may allow one to start unilaterally; however, performing a CTO recanalisation without displaying the distal coronary target is irresponsible. Indeed, dual injection allows better visualisation and understanding of CTO morphology and complexity. In addition, it can improve procedural safety by elucidating guidewire location during crossing attempts. CTO PCI with a single guide can be performed in selected cases with absent collateral circulation or only ipsilateral collateralisation.

Most operators use 7 Fr guides for recanalisation and 5 or 6 Fr guides for contralateral injection[47]. We recommend the use of guide catheters with side holes to prevent forceful intraplaque injections that may easily cause spiral dissections and also to allow proper monitoring of the arterial pressure. For the left coronary artery, extra backup guides (EBU) are most appropriate; sometimes Amplatz left curves are valid alternatives for the circumflex artery. For the right coronary, Judkins right or Amplatz left (AL1 or AL 2) represent the most employed catheters, while internal mammary artery (IMA) guides, shepherd's crook (SC) or hockey stick curves are useful for SC origin engagement. The operator should be familiar with deep intubation, anchoring balloon and mother-and-child techniques (guide-in-guide). The various choices for access are: bifemoral artery, biradial (or ulnar) artery[48], radial and femoral, and two ipsilateral femoral sheaths[49]. While the radial approach appears more cumbersome, especially in very complex CTO procedures, none of the approaches was shown to be superior to any other[48].

Regarding perprocedural anticoagulation, an initial bolus of intravenous unfractionated heparin (100 IU/kg) is generally administered. The activated clotting time is then monitored every 30 minutes to determine whether an additional bolus of unfractionated heparin is necessary to maintain an activated clotting time >250-300 s. Upstream use of low molecular weight heparin, glycoprotein IIb/IIIa inhibitor therapy or bivalirudin is generally not recommended.

ANTEGRADE APPROACH

The antegrade approach, and particularly antegrade wire escalation (AWE), remains the cornerstone of CTO PCI, being performed in approximately three quarters of cases[50,51]. All experts agree that AWE is the strategy of choice in case of non-ambiguous proximal cap, good distal landing zone, and lesion length <20 mm. Indeed, a true-to-true lumen approach – when feasible – seems recommendable, as extensive vessel disruption with dissection/re-entry techniques is associated with greater intravascular ultrasound (IVUS)-detected vascular injury, angiographic dye staining/extravasation, branch occlusion, and periprocedural myocardial infarction[52]. However, the clinical significance of such findings is debated, since no clear evidence of the superiority of a true-to-true approach has been demonstrated so far[53,54]. The choice of microcatheters and guidewires depends on operator preference and specific angiographic features: in general, highly manoeuvrable guidewires with 1:1 torque response are recommended as initial choices (e.g., Gaia family, Fielder XT-R; FIGHTER™ [Boston Scientific, Marlborough, MA, USA]) to maintain an intra-plaque track. If a subintimal situation at the landing zone is observed, a wide array of techniques for true lumen re-entry is available. These encompass both wire-based and device-based (Stingray™; Boston Scientific) re-entry[55]. Among wire-based techniques, preference should be given to those providing targeted re-entry[56] (e.g., parallel wires, mini-STAR, limited antegrade subintimal tracking, IVUS-guided re-entry …). Alternatively, antegrade dissection/re-entry (ADR) is suggested by some operators as a first-line strategy. This is usually performed in case of ambiguous proximal cap, adequate distal landing zone, and occlusion length >20 mm. In this setting, the CrossBoss™ (Boston Scientific) is recommended by some operators, since this catheter is meant to create a smaller subintimal space disruption compared with knuckle wires. Subsequently, Stingray-based re-entry may be performed.

RETROGRADE APPROACH

The retrograde approach should be considered in occlusions with "interventional" collaterals (i.e., collaterals deemed to be negotiable by the operator depending on his/her experience), diseased landing zone, bifurcation at distal cap, and/or proximal cap ambiguity[57]. Dedicated microcatheters and guidewires should be used; the utilisation of OTW balloons and guidewires not specifically designed for collateral crossing should be avoided. Preference should be given to septal collaterals (due to lower risk in case of perforation as compared with epicardial channels)[50,57,58] and diseased/occluded saphenous vein grafts (which do not present side branches and therefore allow easy navigation)[58]. Epicardial collaterals should be considered only by very experienced operators and, in any case, as a second-line option[59]. Fortunately, septal channels are most frequently found in both right coronary artery (72%) and left anterior descending (52%) CTOs[60]. However, circumflex CTOs most frequently present ipsilateral epicardial collaterals, which should be tackled with great care, utilising dedicated wires (e.g., SUOH 03, SION black; both Asahi Intecc) and techniques (e.g., tip injection to delineate vessel course, rendezvous or tip-in for externalisation, etc.). In any case, specific complication-solving skills are needed when undertaking the

retrograde approach, including pericardiocentesis, coiling, covered stent implantation, and establishing haemodynamic support. With regard to the procedural techniques specific to the retrograde approach, although retrograde true-to-true wire crossing is ideally pursued in cases of short, non-calcified occlusions, reverse controlled antegrade and retrograde subintimal tracking (CART) is effectively performed in the majority of cases[50,61]. The recently introduced concept of "directed reverse CART" seems promising to maximise the effectiveness of this technique while limiting the extent of vessel damage. In directed reverse CART, close proximity between the antegrade and retrograde wires is achieved, before performing balloon dilatation with a small balloon (usually 2.0 mm). Then, a highly manoeuvrable retrograde wire (e.g., Gaia) is carefully manoeuvred towards the (lateral side of the) antegrade balloon, thus creating a connection between the retrograde and antegrade systems. If there is difficulty in making the connection, the use of IVUS should be considered to understand the antegrade and retrograde wire position[62]. Finally, in long occlusions with ambiguity or unclear vessel course and severe calcifications, a retrograde knuckle wiring (with polymer-jacketed guidewires) facilitates overcoming the occluded segment with a low risk of perforation.

THE CONCEPT OF THE "HYBRID ALGORITHM"

The integration of the aforementioned techniques into a homogeneous set of strategies has become known as the "hybrid algorithm"[57]. This approach was developed by North American operators in 2012 and is based on the concept of a rapid switch from one approach to another in case of low likelihood of success, in order to optimise procedural efficiency. After dual coronary angiography, four angiographic parameters are assessed: 1) proximal cap location and (non-) ambiguity; 2) occlusion length; 3) quality of the distal vessel; 4) presence of collaterals suitable for retrograde techniques ("interventional collaterals"). Based on these four features, an initial strategy and hierarchy for subsequent approaches are established. The hybrid algorithm has been shown

to be effective (success rates of ~90%), safe (low rates of complications: tamponade 1.3%, periprocedural myocardial infarction 1.0%, death 0.4%), and efficient (favourable procedural metrics)[50]. Additionally, the mantra of this algorithm is its reproducibility and the fact that it can be easily taught/learned, resulting in high success rates obtained by new operators[63].

Recently, the Asia Pacific Chronic Total Occlusion Club developed a modified hybrid algorithm for CTO PCI[35]. Despite similarities with the traditional hybrid algorithm, major changes exist in this new algorithm: i) the role of IVUS-guided entry to overcome proximal cap ambiguity is clearly highlighted; ii) the CTO length alone does not determine the choice of either a wire escalation strategy or a dissection re-entry strategy; iii) the use of the parallel wire technique and IVUS-guided wiring as a bail-out strategy in the antegrade arm; iv) the CrossBoss catheter should be considered as the first-line device for in-stent CTO recanalisation[35].

In **Figure 3**, we propose a modified hybrid algorithm for CTO PCI using the contemporary techniques.

Intravascular imaging in CTO PCI

The section on IVUS[62,64,65] can be found in **Supplementary Appendix 3**.

The section on OCT[66,67] can be found in **Supplementary Appendix 4**.

Stents in CTO PCI

After successful recanalisation of CTOs, implantation of drug-eluting stents (DES) reduces the rates of major cardiac events, restenosis and stent re-occlusion as compared to bare metal stents[68]. Everolimus-eluting (EES) and zotarolimus-eluting stents (second-generation DES) are currently preferred for CTO interventions as they enable better outcomes compared to the first generation of DES[69-73] **(Table 2)**. Although the BIOFLOW V study showed superiority of a hybrid ultra-thin sirolimus-eluting stent (SES) compared with EES, this finding was not confirmed in the PRISON IV study (non-inferiority for in-segment late

Table 2. Comparison of published prospective studies on the clinical and angiographic outcomes with new-generation DES in CTOs.

Study	Year	DES	N	FU angio time (months)	Prior CABG (%)	Total stent length (mm)	In-stent restenosis (%)	In-segment restenosis (%)	TLR (%)	TVR (%)
CIBELES[69]	2012	SES	101	9	4	47±24	NR	10.5	7.5	11.6
		EES	106	9	4.7	50±23	NR	9.1	6.0	7.9
CATOS[70]	2012	SES	80	9	NR	44.6±20.2	NR	13.7	NR	13.8
		Endeavor ZES	80	9	NR	43.4±21.5	NR	14.1	NR	7.5
PRISON III[71]	2012	SES	60	8	5.0	38.4±18.4	2.0	12.0	6.7	8.3
		Endeavor or Resolute ZES	62	8	8.1	41.0±19.2	5.5	10.9	4.8	4.8
ACE-CTO[72]	2015	EES	100	8	27	85±34	46	46	37	39
EXPERT CTO[73]	2015	EES	222	12	9.9	52±27	NR	NR	6.3	NR

CABG: coronary artery bypass graft surgery; CTO: chronic total occlusion; DES: drug-eluting stents; EES: everolimus-eluting stents; FU: follow-up; NR: not reported; SES: sirolimus-eluting stents; TLR: target lesion revascularisation; TVR: target vessel revascularisation; ZES: zotarolimus-eluting stents
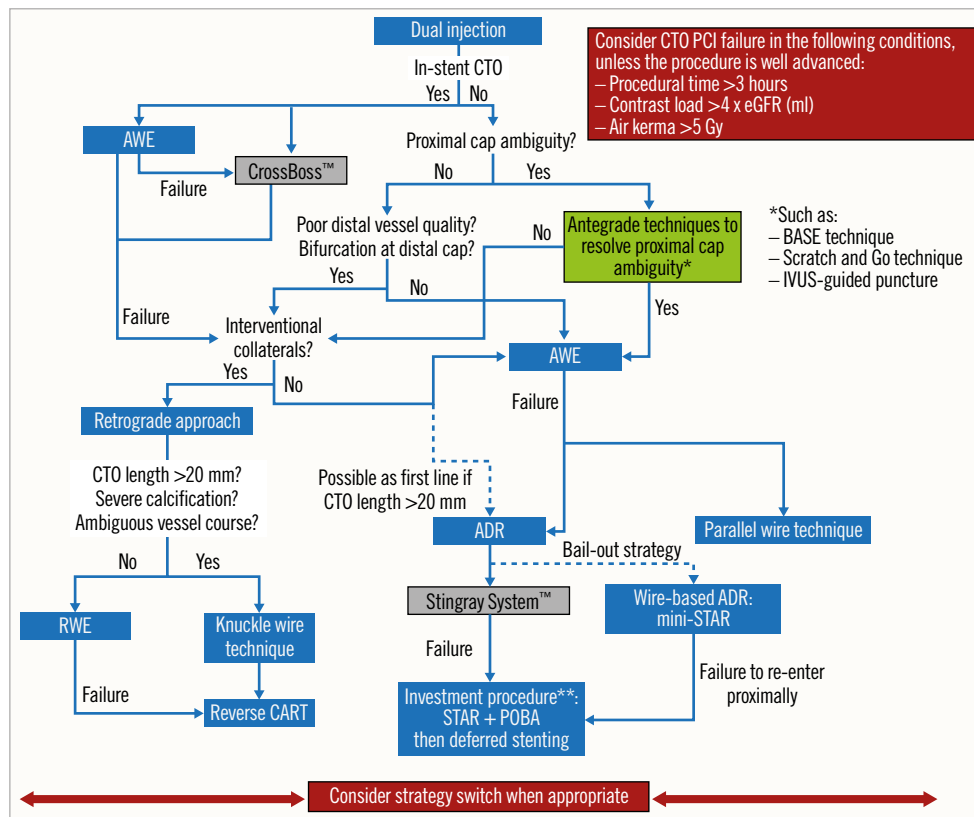
Figure 3. *Modified hybrid algorithm for CTO PCI. **Investment procedure refers to deferred stenting (during a second procedure) after subintimal plaque modification via the STAR technique and balloon dilatation[43]. ADR: antegrade dissection re-entry; AWE: antegrade wire escalation; BASE: balloon-assisted subintimal entry; CART: controlled antegrade retrograde tracking; CTO: chronic total occlusion; eGFR: estimated glomerular filtration rate; IVUS: intravascular ultrasound; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty; RWE: retrograde wire escalation; STAR: subintimal tracking and re-entry*

lumen loss not reached, and a higher rate of binary restenosis in the hybrid SES group)[74,75]. The promising concept of this stent design needs further research in CTO lesions. In the EUROCTO trial, biolimus-eluting stents with abluminal biodegradable polymer were used with satisfactory one-year outcome (ischaemia-driven revascularisation – 2.9%)[32].

Although the concept of biodegradable scaffold use in CTOs appeared to be attractive, they are actually no longer recommended for clinical use. Some authors have also proposed the concept of using drug-coated balloons without stent implantation in CTO PCI; however, this needs further evaluation.

CTO in particular settings

Supplementary Appendix 5 is dedicated to CTO PCI in the following particular settings: CTO associated with bifurcation lesions[76-78], in-stent CTO[79-83] and CTO patients with low left ventricular ejection fraction (LVEF)[27,84-86].

Immediate outcome, complications and safety issues

The results of opening a CTO are mainly operator-dependent as well as being driven by a few patient- and morphology-related parameters. Our experience, now with far more than 20,000 procedures in the monitor-reviewed online registry of the EuroCTO club, shows that operators who performed more than 300 CTOs and maintain an annual procedure number of at least 50 cases will have a success rate of more than 85%, which is still lower than that of non-occlusive lesions[51]. As success rates have increased during recent years, the rate of major complications has decreased to less than 2% and appears close to that of PCI of non-occluded coronary arteries[62]. Periprocedural myocardial injury discovered by measurement of cardiac biomarkers may occur in 5-10% of the patients, is more common with the retrograde approach and is associated with worse clinical outcome at follow-up[87]. Aortocoronary dissection may occur in <1% of CTO PCI attempts[88]; the therapeutic strategy and outcome depend on the rapidity of the entry point sealing and the degree of extension of the dissection[89]. Donor vessel injury during retrograde CTO PCI requires rapid identification and management, since it is frequently associated with extensive ischaemia and haemodynamic instability[90]. Small perforations and pericardial effusions are more likely to occur (3-5%)[51,89], but are uneventful if addressed rapidly and properly[89-93]. **Figure 4** and **Supplementary Appendix 6** focus on the management of coronary perforations during CTO PCI attempts.
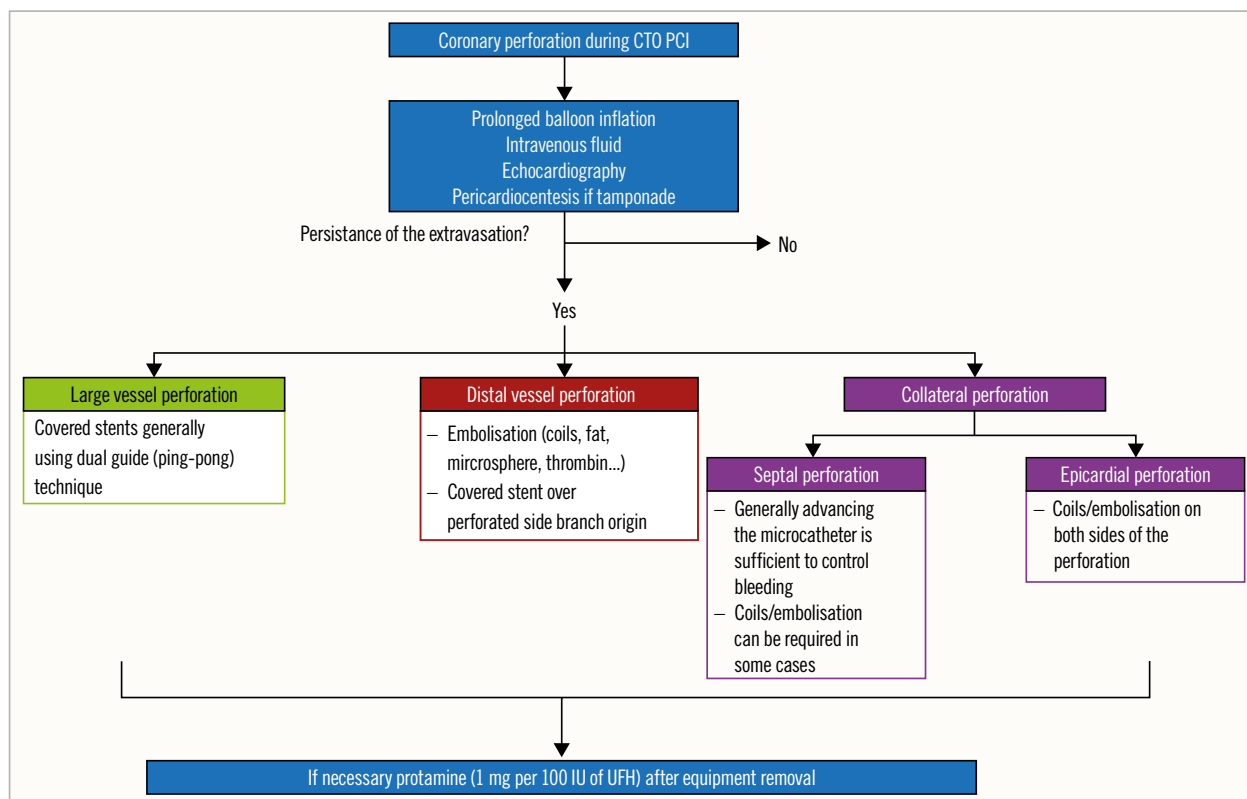
Figure 4. *Management of coronary perforation in CTO PCI. CTO: chronic total occlusion; UFH: unfractionated heparin; PCI: percutaneous coronary intervention*

The section on radiation and contrast use[94-97] can be found in **Supplementary Appendix 7**.

Dual antiplatelet therapy (DAPT) after CTO PCI

Dual antiplatelet therapy (DAPT) for at least six months is currently recommended post-stenting in patients with stable ischaemic heart disease (class I recommendation)[98]. Prolonged (up to 30 months) DAPT duration may be considered (class IIb recommendation) in patients who have undergone complex PCI[98]. The optimal duration of DAPT in patients who underwent CTO PCI, considered to be at higher ischaemic risk, remains unknown. In a meta-analysis of six RCTs, Giustino et al[99] showed that longer DAPT duration after PCI (>12 months) was not associated with improved clinical outcomes in CTO patients, differently from other subsets of complex non-CTO PCI, such as long stent length (>60 mm), two-stent bifurcation technique and ≥3 stents implanted. In another retrospective study, Lee et al[100] showed no differences in the incidence of major adverse cardiac and cerebrovascular events or moderate to severe bleeding between CTO patients taking >12-month DAPT and those switched to single antiplatelet therapy after 12 months.

Hence, in the absence of strong clear evidence, DAPT in CTO patients undergoing PCI should be prescribed on a tailored (case-by-case) basis and the duration should be indicated according to the clinical presentation and the assessment of both ischaemic and bleeding risks[98].

How to set a CTO programme

Supplementary Appendix 8 focuses on the learning/training process in CTO PCI as well as centre requirements and centre/operator qualifications.

Conclusion

During recent years, major advances have been achieved in the field of CTO PCI. The current updated consensus summarises the contemporary European practice in CTO PCI influenced by the development of dedicated material and the growing expertise among European CTO operators. The aim of the EuroCTO Club is to contribute actively to the training of interventional cardiologists in contemporary CTO techniques in order to achieve high levels of success, low rates of complication and to improve the outcome of CTO patients.

Conflict of interest statement

L. Azzalini reports research grants from Abbott Vascular, ACIST Medical Systems, Guerbet, and Terumo, and honoraria from Guerbet, Terumo and Sahajanand Medical Technologies. A. Avran reports honoraria from Abbott Vascular, Boston Scientific, Biosensors, Terumo and Biotronik for teaching courses and proctoring. A. Gershlick has received travel sponsorship and speaker's fees from Abbott Vascular and Medtronic. C. Di Mario reports speaker's fees from Philips Volcano. The other authors have no conflicts of interest to declare.

References

The complete list of references can be found in the online version of this paper.

Supplementary data

Supplementary Appendix 1. Overview of the characteristics and use of some microcatheters.
Supplementary Appendix 2. Support catheters and guide extension catheters.
Supplementary Appendix 3. Intravascular ultrasound (IVUS).
Supplementary Appendix 4. Optical coherence tomography (OCT).
Supplementary Appendix 5. CTO and bifurcation lesions.
Supplementary Appendix 6. Coronary perforations and their management in CTO PCI.
Supplementary Appendix 7. Radiation and contrast use.
Supplementary Appendix 8. Learning and training in CTO PCI.
Supplementary Table 1. An overview of CTO guidewires.
Supplementary Table 2. Available dual lumen microcatheters and support catheters for CTO PCI.
Supplementary Table 3. Guide extension catheters.

The supplementary data are published online at:
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Supplementary data

Supplementary Appendix 1. Overview of the characteristics and use of some microcatheters.

Corsair and Corsair Pro

The Corsair microcatheter (Asahi Intecc) is composed of eight thin wires wound with two larger wires, to facilitate torque transmission. The inner lumen is lined with a polymer allowing contrast injection and wire advancement. The distal 60 cm are coated with a hydrophilic polymer to improve crossability. A platinum marker coil is placed 5 mm from the tip.

In the Corsair Pro (Asahi Intecc) the distal radiopaque marker band was removed, the tip flexibility was enhanced, and the hub was redesigned to encompass the proximal section of the catheter, reducing the likelihood of guidewire kinking and entrapment.

The Corsair catheter can be advanced by rotating in either direction, although better torque transmission is obtained with counter-clockwise rotation. However, the Corsair should not be over-rotated (>10 consecutive turns without release), as this can lead to catheter deformation and entrapment, and fracture proximal to the catheter tip, or result in the wire binding to the microcatheter (Corsair "fatigue").

Caravel

The Caravel microcatheter (Asahi Intecc) was designed for crossing small and tortuous collaterals. It has a very low distal tip profile, a braided shaft and low distal shaft profile with a hydrophilic coating. It can be either advanced with forward push or rotated to cross tortuous collaterals. Importantly, aggressive rotation and advancement should be avoided because it may strain the distal tip connection to the shaft and result in fracturing of the Caravel tip.

Finecross

The Finecross (Terumo) microcatheter is very flexible and navigates well through tortuosity thanks to its low crossing profile. Its stainless steel braid tends to enhance its torquability; a distal marker is located 0.7 mm from the tip of the microcatheter. The Finecross is generally advanced using forward push; however, a combination of push and rotation can also facilitate its advancement.

MicroCross 14 and MicroCross 14ES

The MicroCross 14 (Roxwood Medical [now BTG]) microcatheter is the longest (155 cm long) and one of the lowest crossing profile microcatheters (1.6 Fr distal tip) available in the market. It has variable pitch braid, a hydrophilic coating and is designed to advance mainly by pushing. The MicroCross 14 is more flexible for advancing through tortuosity or for retrograde approach, while the MicroCross 14ES (extra support) is more suitable for enhanced antegrade crossing.

Turnpike, Turnpike LP, Turnpike Spiral, Turnpike Gold

The Turnpike (Vascular Solutions) has a dual-layer bidirectional coil that facilitates torque transmission while allowing flexibility and preventing kinking. It also has a soft, tapered tip suitable for crossing collaterals.

Turnpike is the standard catheter with a 1.6 Fr outer diameter at the distal tip and 2.6 Fr outer distal shaft diameter. Turnpike LP is a lower-profile version with a 1.6 Fr outer diameter at the distal tip and 2.2 Fr outer distal shaft diameter; it is particularly suitable for crossing very tortuous collaterals (septals, epicardials). The Turnpike Spiral has a distal nylon coil, which "anchors" the microcatheter after advancement and makes it ideal to cross difficult collaterals that might sustain a certain degree of injury (septals and bypass grafts). The Turnpike Gold has a gold-plated, threaded metallic tip and distal nylon coil to increase trackability. Similar to the Tornus (Asahi Intecc), the Turnpike Spiral and Turnpike Gold are well suited for crossing balloon uncrossable lesions. All Turnpike microcatheters are available in 135 and 150 cm lengths, except the Turnpike Gold, which is only available in the 135 cm length.

The Turnpike and Turnpike LP catheters can be rotated in either direction, whereas the Turnpike Spiral and Turnpike Gold are rotated clockwise to advance and counter-clockwise for withdrawal (opposite direction compared with the Tornus catheter).

Supplementary Appendix 2. Support catheters and guide extension catheters

Support catheters

The support catheters are dedicated devices that have a stabilising self-expanding scaffold (MultiCross and CenterCross; Roxwood Medical [now BTG]), an atraumatic elastomeric balloon (Prodigy; Radius Medical) or nitinol struts (NovaCross; Nitiloop) that are deployed proximal to the target CTO lesion. These systems were designed to increase the backup support and the penetration force to cross the proximal cap and traverse through the occlusion. However, their use remains not yet consensual among CTO experts.

Guide extension catheters

Guide extension catheters (GEC) were initially introduced to facilitate device delivery in non-CTO PCI. They can be useful for increasing support during antegrade approach, but also for facilitating stent delivery in tortuous and calcified CTOs. During retrograde approach, mainly the reverse CART technique, GEC can facilitate retrograde wire advancement into the antegrade guiding catheter (by moving the "base of operations" closer to the retrograde gear), enabling wire externalisation (guide extension-facilitated retrograde approach). Most recently, 5 Fr GEC have been commercially available (Guidion; IMDS), enabling a trapping technique inside 8 Fr guiding catheters during single guide retrograde approach. A novel GEC with capability of wire trapping has lately been introduced to facilitate further the exchange of interventional devices during CTO PCI (TrapLiner; Teleflex) and became commercially available in Europe in March 2018.

Supplementary Table 3 summarises the currently available guide extension catheters.

Supplementary Appendix 3. Intravascular ultrasound (IVUS)

Randomised trials have demonstrated that IVUS improves the outcome of CTO PCI in terms of MACE and definite/probable stent thrombosis [64,65], probably thanks to better stent optimisation. Moreover, IVUS has essential roles in both anterograde and retrograde approaches. In the antegrade approach, IVUS has multiple uses, particularly in case of stumpless CTO lesions with proximal cap ambiguity [62]. The IVUS probe can be advanced into a side branch, and during pullback the precise location and morphologic characteristics of the proximal cap of the occlusion can be identified. Thus, through an on-line IVUS guidance, the CTO wire position can be monitored and the entry of the guidewire (ideally centrally) in the proximal cap can be documented. A second use of IVUS is for antegrade re-entry from subintimal space. In this very complex situation, after a previous failed re-entry attempt, the IVUS probe should be inserted on the subintimal guidewire, in order to identify the correct direction for a stiffer guidewire to puncture and to gain the true lumen distally to the occlusion.

In retrograde approach, the IVUS probe, advanced on an anterograde guidewire, can be useful in two situations: retrograde guidewire crossing and reverse CART technique. In the retrograde wire crossing IVUS could be useful in the ostial occlusions or bifurcations with blunt stump. The IVUS probe should be placed immediately in the very ostial segment to visualise the exact location of the retrograde guidewire and its re-entry in the true lumen. The IVUS evaluation is crucial, in particular in case of ostial left anterior descending or circumflex CTO to avoid left main dissection or side branch occlusion. When retrograde guidewire crossing is unsuccessful, an antegrade subintimal dilation to create a connection channel in the same space between antegrade and retrograde guidewires is mandatory to achieve success. In such a situation, IVUS permits the evaluation of antegrade and retrograde guidewire position (both intimal and subintimal or in different spaces), and the selection of the appropriate balloon sizing for medial disruption. In addition, IVUS can be helpful to select the appropriate position for creating connection (more proximally or more distally) when an initial reverse CART strategy is unsuccessful due to severe calcification [62].

Supplementary Appendix 4. Optical coherence tomography (OCT)

Optical coherence tomography (OCT) provides high-resolution cross-sectional images that could help in assessing the degree of intima, media, and fibrous cap thickness of an atherosclerotic plaque and give details of plaque morphology. OCT can further be used to determine lesion length, vessel diameter, length of subintimal track, and the constituents of the arterial wall [66]. Hence, OCT might be used to determine stent length more accurately, limiting inadequate stent expansion or incomplete stent strut apposition, thus minimising the risk for stent thrombosis or restenosis. Indeed, high rates of stent strut malapposition and incomplete stent strut coverage have been reported after CTO PCI [67].

Nonetheless, the lack of clinical data on OCT use in CTO PCI in addition to the need for repeated contrast injections and pullbacks are factors against extending its use in CTO procedures, considering that this can be particularly deleterious in cases where dissection/re-entry techniques have been performed (extension of dissection planes).

Supplementary Appendix 5. CTO and bifurcation lesions

Bifurcation lesions are found in approximatively 25-30% in the context of CTO PCI [76,77], and represent an additional challenge for the interventional cardiologist. The presence of a bifurcation lesion within the CTO target vessel was demonstrated to increase the complexity of the procedure and may lead to less angiographic success and more periprocedural complications [77]. Although it is well established that the one-stent technique is the gold standard for bifurcation treatment in non-CTO lesions, the appropriate strategy to manage bifurcation in the context of CTO PCI remains debatable. Ojeda et al [76] claimed that bifurcation lesions in CTO can be approached similarly to regular bifurcation lesions, for which provisional stenting is considered the technique of choice. However, the side branch stenting rate seems to be higher (15.6%) than in previous non-CTO series [76]. After adjusted analysis, there were no differences in midterm outcomes between the T-provisional stenting (1-stent technique) and two-stent techniques [76]. To the best of our knowledge, only one randomised study has investigated the appropriate strategy for bifurcation lesions located within a CTO vessel. Baystrukov et al [78] showed that, in comparison with T-provisional stenting, the mini-crush technique appeared to be associated with better one-year clinical and angiographic outcomes, particularly when used to treat bifurcation lesions located within the CTO body or close to the proximal or the distal cap (≤5 mm).

The presence of a dissection affecting the bifurcation site in CTO PCI might prevent side branch wiring; in such a scenario dual-lumen microcatheters could be of interest to manage the bifurcation lesion appropriately. Otherwise, in case of the antegrade dissection re-entry technique with no possibility to achieve re-entry before SB take-off, the retrograde approach might be an interesting alternative to preserve both branches.

In-stent CTO

In-stent CTOs represent 11-12% of all CTO PCIs [79,80]. These procedures are often more complex than those in unstented vessels, due to the resistance offered by restenotic fibrocalcific tissue and the close proximity of stent struts with microcatheters, wires and balloons, as well as the need to maintain a within-stent track. In-stent CTOs present similar angiographic complexity compared with de novo occlusions [79]. The CrossBoss catheter (Boston Scientific) is particularly useful to cross long stented segments quickly, avoiding exit into the subadventitial space [81]. Success rates for in-stent CTO PCI were historically lower

than for *de novo* lesions but have recently reached similar figures (86-87% vs. 87-90% [79,80]).

However, long-term follow-up reveals a threefold increase in the risk of target vessel revascularisation for patients with in-stent CTOs, mirroring similar findings in non-occlusive disease, where PCI for in-stent restenosis had been identified as a predictor of future restenotic events [79]. For this reason, use of intravascular imaging to identify the cause of restenosis, guide stent choice, and optimise the final result is of the utmost importance.

Although a within-stent track is the recommended approach to recanalise in-stent CTOs, sometimes this is impossible to achieve, and subadventitial crossing with subsequent crushing might represent the only feasible option [82]. This approach has recently been proposed to treat very complex occlusions, after failure of within-stent techniques. Subadventitial crossing appears to be effective and safe, and is associated with acceptable outcomes on mid-term follow-up, which are similar to those achieved using within-stent techniques [83]. However, subadventitial crossing and crushing of occluded stents should be considered only as a last resort by very experienced operators, since it is technically demanding, not devoid of complications (e.g., perforation), and its long-term outcomes are poorly characterised.

CTO in patients with impaired left LVEF

Current guidelines and appropriate use criteria for myocardial revascularisation do not provide any recommendation regarding the most appropriate management strategy in CTO patients with low LVEF [27]. Severe ischaemic left ventricular dysfunction is associated with higher morbidity, an increased risk of sudden death due to ventricular arrhythmias, poor quality of life, and frequent re-hospitalisation for heart failure. Successful CTO PCI in these patients is associated with significant improvement of LVEF and symptoms at six-month follow-up and also improves the midterm clinical outcome [84]. Although CTO PCI represents an efficient as well as safe strategy in patients with low LVEF, important precautions have to been taken before treating this subgroup of patients. Particularly in patients with acute left heart failure and/or retrograde PCI over a last remaining vessel, additional haemodynamic support such as an intra-aortic balloon pump, Impella® device (Abiomed, Danvers, MA, USA) or even an extracorporeal life support system may be mandatory during the procedure [85,86].

Supplementary Appendix 6. Coronary perforations and their management in CTO PCI

Coronary perforation represents one of the most feared complications of CTO PCI, as it can be responsible for pericardial effusion and tamponade, requiring emergency pericardiocentesis, and in some cases cardiac surgery. Coronary perforation is generally located within the target CTO vessel (either the main vessel or its distal segment) or in the collateral supplying the CTO territory. Although coronary perforations are relatively common [89,90], the risk of tamponade is low (~0.3%) [89]. This risk is higher with retrograde CTO PCI (1.3%) [91], particularly when epicardial collaterals are used [89].

While small perforations can be managed conservatively, those causing pericardial effusion often require appropriate measures to stop bleeding into the pericardium.

Generally, a semi-compliant balloon (sized the same as the vessel) should immediately be inflated (8-10 mm) proximal to the perforation. In case of haemodynamic instability, immediate pericardiocentesis is required, while small size pericardial effusion (without haemodynamic collapse) is preferably managed conservatively. Anticoagulation reversal (generally with 1 mg protamine per 100 IU of UFH) should not be performed until the equipment removal to avoid catheters and vessel thrombosis.

If the extravasation persists in spite of prolonged balloon inflation, further measures [92,93] should be applied, depending on the vessel size and the perforation location, as shown in **Figure 2**.

If different percutaneous attempts fail, cardiac surgery remains the last alternative to stop bleeding.

Importantly, coronary perforations in patients with prior CABG can be lethal as they may lead to loculated effusions that compress cardiac structures and are challenging to drain percutaneously [91].

Supplementary Appendix 7. Radiation and contrast use

We strongly believe that radiation injury to the skin (reported to be 0.42%) [94], as well as contrast-induced kidney injury (CIN) that probably occurs in up to 10% [95] are both underreported complications. The average amount of radiation dose in CTO procedures measured as air kerma is 3-6 Gy and 2-4 times that of non-CTO lesions PCI [96], while contrast load averages 350 ml, which is 150-200 ml more than required for PCI of non-occlusive disease [97]. Excessive dye consumption and radiation exposure are both mainly driven by lesion complexity, operator experience, radiation habits and cath lab settings (low pulse frequencies, e.g., 7.5 pulses per second instead of 15-30). Since the amount of dye that will be required may not be predictable, we recommend i.v. hydration with isotonic saline one day prior to and 12 hours after the procedure for all patients with chronic kidney disease (eGFR <60 ml/min/1.73 m²) and consider it also for CTO patients irrespective of their eGFR.

Supplementary Appendix 8. Learning and training in CTO PCI

Learning CTO PCI can be achieved either through a formal fellowship programme or through "on the job" training, while practising. Both can provide excellent training; however, high procedural volume is required as it does correlate with skills [50].

A multifaceted approach to learning CTO PCI is advised. Reading CTO-related literature represents the knowledge base upon which all subsequent learning should be built. Attending CTO courses and meetings allows sharing of experience and challenging scenarios delivered by expert operators, as well as facilitating professional networking with experts. Moreover, interaction through social media and online communities promotes constant sharing of experiences with peers. Finally, getting proctored by experienced CTO interventionalists ("on the job training") is an invaluable resource for learning CTO PCI.

The basic set of techniques for developing expertise in CTO PCI is represented by antegrade wire escalation. Then, the operator interested in developing his/her CTO skills further can embrace two paths: ADR or the retrograde approach. ADR is favoured by the so-called "hybrid" operators and represents a technically less demanding approach compared with retrograde techniques. Embracing the retrograde approach requires acquisition of specific material (microcatheters, wires, snares, etc.), learning several different techniques to deal with each step from collateral channel engagement to wire externalisation, as well as being prepared to deal with complications (e.g., perforation, tamponade, donor vessel ischaemia, etc.). With regard to collateral channel choice, it might be advisable to start tackling bypass grafts and septal channels first, before embarking on retrograde CTO PCI via epicardial collaterals, which present higher risk for rupture.

Centre requirements

At the logistics level, deliberate support from the hospital administration is key to setting up a successful CTO PCI programme. This involves availability to acquire dedicated material for CTO intervention, designation of specific CTO operators (one or ideally two) and "CTO days", and an outreach programme to build and foster a strong network of referring physicians [2]. Cath lab leadership should strive to promote training not only among CTO PCI interventionalists, but also among nurses and technicians. Specific protocols to manage CTO-specific issues during the procedure should be set up and implemented. These include: checking activated clotting time at regular intervals (e.g., every 30 minutes), warning the

operator(s) when specific thresholds of contrast volume and radiation dose are reached, managing patients' complaints related to long procedures (back pain, urination, etc.), and so on. While specific gear (e.g., retrograde wires, snares, etc.) related to specific approaches of CTO PCI are not necessarily must-haves for all CTO PCI programmes (e.g., those initially willing to focus on antegrade techniques exclusively), it is mandatory that every cath lab where CTO recanalisation is performed owns certain devices needed to solve life-threatening complications (and the skills needed to use them). These include coils and covered stents to deal with perforation, pericardiocentesis kit to relieve tamponade, and mechanical circulatory support devices (at least intra-aortic balloon pump) for assistance in case of ischaemic complications. Finally, on-site surgical back-up ought not to be mandatory, but the appropriateness of indications must be confirmed by the regular involvement of a "Heart Team" including cardiac surgeons.

Centre/operator expertise

A direct relationship between case volume and success rate exists for CTO PCI. In fact, it has been shown that at least 100 CTO PCIs/year must be performed by an operator to reach a success rate >90% [50]. While achieving such high volumes might be challenging for most institutions and operators, we strongly believe that centres and operators performing fewer than 30 CTO procedures annually should refer their CTO patients to a more experienced operator [2].

Retrograde techniques should be reserved for experienced operators (i.e., those performing >50 per year). A minimum of 50 retrograde procedures (25 as second operator and 25 as first under supervision) might be advised before a cardiologist becomes an independent retrograde operator [2].

Corrigendum to "Percutaneous recanalisation of chronic total occlusions: 2019 consensus document from the EuroCTO Club"

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Accordingly, we have now corrected the Online Supplemental Material 1 of the EuroCTO club Consensus

Online Supplemental Material 1. An overview of CTO guidewires

Guidewire		Wire diameter (inch/mm)	Tip stiffness (g)	Polymeric	Hydrophilic tip	Hydrophilic shaft
Abbott Vascular	Cross-It™ 100	0.014"/0.35 mm Tapered tip 0.010"/0.26 mm	1.7	N	N	N
	Cross-It™ 200	0.014"/0.35 mm Tapered tip 0.010"/0.26 mm	3	N	N	N
	Cross-It™ 300	0.014"/0.35 mm Tapered tip 0.010"/0.26 mm	4	N	N	N
	Cross-It™ 400	0.014"/0.35 mm Tapered tip 0.010"/0.26 mm	6	N	N	N
	Whisper LS, MS, ES™ (Light, Medium, Extra Support)	0.014"/0.35 mm	0.8,1.0 and 1.2	Y	Y	N
	Pilot™ 50	0.014"/0.35 mm	1.5	Y	Y	N
	Pilot™ 150 and 200	0.014"/0.35 mm	2.7 and 4.1	Y	Y	Y
	Progress 40	0.014"/0.35 mm	4.8	N	N	Y
	Progress 80	0.014"/0.35 mm	9.7	N	N	Y
	Progress 120	0.014"/0.35 mm	13.9	N	N	Y
	Progress 140T	0.014"/0.35 mm Tapered tip 0.010"/0.26 mm	12.5	N	N	Y
	Progress 200T	0.014"/0.35 mm Tapered tip 0.009"/0.23 mm	13.9	N	N	Y
Asahi Intecc Corporation	Intermediate™	0.014"/0.35 mm	3	N	N	N
	Miraclebros™	0.014"/0.35 mm	3, 4.5, 6, 9 and 12	N	N	N
	Confianza™	0.014"/0.35 mm Tapered tip 0.009"/0.23 mm	9	N	N	N
	Confianza™ Pro	0.014"/0.35 mm Tapered tip 0.009"/0.23 mm	9.3 and 12.4	N	N	Y
	Confianza™ Pro "8-20"	0.014"/0.35 mm Tapered tip 0.008"/0.20 mm	20	N	N	Y

	Fielder™	0.014"/0.35 mm	1	Y	Y	N
	Fielder™ FC	0.014"/0.35 mm	0.8	Y	Y	N
	Fielder™ XT	0.014"/0.35 mm Tapered tip 0.009''/0.23 mm	0.8	Y	Y	N
	Fielder™ XT-A	0.014"/0.35 mm Tapered tip 0.010''/0.26 mm	1.0	Y	Y	N
	Fielder™ XT-R	0.014"/0.35 mm Tapered tip 0.010''/0.26 mm	0.6	Y	Y	N
	Decillion FL™	0.010"/0.26 mm	0.8	N	Y	N
	Decillion HS™	0.010"/0.26 mm	1.5	Y	Y	N
	Decillion MD™	0.010"/0.26 mm	3.0	N	Y	N
	SION™	0.014"/0.35 mm	0.7	N	Y	Y
	SION blue™	0.014"/0.35 mm	0.5	N	N	Y
	SION blue ES™	0.014"/0.35 mm	0.5	N	N	Y
	SION black™	0.014"/0.35 mm	0.8	Y	Y	Y
	SUOH 0.3™	0.014"/0.35 mm	0.3	Y	Y	Y
	GAIA First	0.014"/0.35 mm Tapered tip 0.010''/0.26 mm	1.7	N	Y	Y
	GAIA Second	0.014"/0.35 mm Tapered tip 0.011''/0.28 mm	3.5	N	Y	Y
	GAIA Third	0.014"/0.35 mm Tapered tip 0.012''/0.30 mm	4.5	N	y	Y
	RG3	0.010''/0.26 mm	3.0	N	Y	Y
Boston Scientific	Choice™ PT and PT2 LS and MS	0.014"/0.35 mm	2.1	Y	Y	Y
	PT Graphix™ Intermediate Graphix P2™ LS and MS	0.014"/0.35 mm	1.7 and 2.9	Y	Y	Y
	Marvel™	0.014"/0.35 mm	0.9	N	Y	N

Manufacturer		Diameter				
	Samurai™	0.014"/0.35 mm	0.5	N	Y (reduced on distal 1cm)	N
	Samurai RC™	0.014"/0.35 mm	0.5	N	Y	N
	Fighter™	0.014"/0.35 mm Tapered tip 0.009''/0.23 mm	1.2	Y	Y	Y
	Hornet™	0.014"/0.35 mm Tapered tip 0.008''/0.20 mm	1.0	N	Y	N
	Hornet 10™	0.014"/0.35 mm Tapered tip 0.008''/0.20 mm	10	N	Y	N
	Hornet 14™	0.014"/0.35 mm Tapered tip 0.008''/0.20 mm	14	N	Y	N
Cordis/ Johnson & Johnson	Shinobi™	0.014"/0.35 mm	7	Y	Y	N
	Shinobi™ Plus	0.014"/0.35 mm	6.8	Y	Y	N
Medtronic	Persuader™ 3 and 6	0.014"/0.35 mm	3 and 6	N	B	N
	Persuader™ 9	0.014"/0.35 mm Tapered tip 0.011"/0.28 mm	9	N	B	N
Terumo	Crosswire NT™	0.014"/0.35 mm	7.7	N	Y	N
	Crosswire™ Hard type 40	0.014"/0.35 mm	15.6	N	Y	Y
	Crosswire™ Hard type 80	0.014"/0.35 mm	26.7	N	Y	Y
	Runthrough™ NS Floppy	0.014"/0.35 mm	1	N	Y	N
	Runthrough™ NS Hypercoat	0.014"/0.35 mm	1	Y	Y	Y
	Runthrough™ NS Intermediate	0.014"/0.35 mm	3.6	N	Y	N
	Glidewire™ Gold Neuro	0.011"/0.27 mm	1	N	Y	Y

Abbreviations

B=both; CTO=chronic total occlusion; N=No; Y=Yes.

Supplementary Table 2. Available dual lumen microcatheters and support catheters for CTO PCI.

Manufacturer	Catheter	Length	Distal shaft outer diameter
IMDS	NHancer Rx	135 cm	2.6 Fr
Kaneka	Crusade	140 cm	1.3 Fr distal tip 3.1 Fr crossing profile
Terumo	FineDuo	140 cm	
Teleflex	Twin-Pass and Twin-Pass Torque	140 cm	1.9 Fr distal tip 3 Fr crossing profile
Asahi Intecc	SASUKE	145 cm	1.5 Fr distal tip 2.5 Fr crossing profile

CTO: chronic total occlusion; PCI: percutaneous coronary intervention

Supplementary Table 3. Guide extension catheters.

Guide extension catheter	Sizes (Fr)	Guide segment	Working length	Coating	Characteristics
Guidion Hydro (**IMDS, the Netherlands**)	5, 6, 7, 8 Fr	25 cm	150 cm	Hydrophilic coating	True visible soft tip. Low distal shaft friction. Lumen with flat wire coil reinforcement.
GUIDEZILLA (Boston Scientific, USA)	6, 7, 8 and 6 Fr long	25 cm on 6 Fr, 7 Fr, 8 Fr (40 cm on 6 Fr long)	150 cm	Hydrophilic coating	Marker 2 mm from distal end. Large-profile proximal shaft. Lumen with braid reinforcement.
GuideLiner (Teleflex, USA)	5, 5.5, 6, 7, 8 Fr and 6 Fr long	25 cm on 6 Fr, 7 Fr, 8 Fr (40 cm on 6 Fr long)	150 cm	Hydrophobic coating	Marker 2 mm from distal end. Lumen with flat wire coil reinforcement.

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