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Reviews

Percutaneous Coronary Intervention of Chronic Total Occlusions: When and How to Treat☆,☆☆

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ABSTRACT

Chronic coronary total occlusions (CTO) are diagnosed in up to 20% of patients with coronary artery disease and have a detrimental effect on patients' quality of life and long-term prognosis. The exponential developments in CTO percutaneous coronary intervention (PCI) equipment, recanalization techniques, and operator expertise have been merged into the hybrid approach that represents a percutaneous revascularization algorithm for treating CTOs and has led to technical success over 90% at experienced centers. Therefore, patient selection for CTO PCI should be focused on anticipated patient benefit in terms of health status and long-term prognosis rather than coronary anatomic complexity.

Table of contents: This review will provide an overview of the clinical presentation and characteristics of patients with a CTO and will discuss the essential needs toward judicious patient selection for percutaneous CTO revascularization according to contemporary knowledge. Furthermore, the current high standard revascularization techniques in dedicated CTO PCI will be discussed.

Contents

Abbreviations: ADR, antegrade dissection and reentry; AWE, antegrade wire escalation; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CART, controlled antegrade and retrograde subintimal tracking; CTO, chronic coronary total occlusions; IRA, infarct-related artery; J-CTO score, Japanese CTO score; LAST, limited antegrade subintimal tracking; LVF, left ventricular function; MI, myocardial infarction; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; RDR, retrograde dissection and reentry; RWE, retrograde wire escalation; STAR, subintimal tracking and reentry; STEMI, ST elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction.

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1. Introduction

Chronic coronary total occlusions (CTO) can be considered the final stage of obstructive coronary artery disease (CAD) and are associated with a negative impact on long-term prognosis [1]. A CTO is defined as a complete luminal obstruction of a native coronary artery for a duration of ≥3 months. The minimal duration of a CTO is preferably determined by previous coronary angiography or, if unavailable, estimated based on clinical grounds [2]. CTOs are classified by the Thrombolysis in Myocardial Infarction (TIMI) flow grade on invasive coronary angiography as a “true” or “functional” CTO (TIMI flow grade 0 and 1, respectively). In large clinical registries, a CTO has been diagnosed in 16–18,4% of patients with CAD [3,4]. These large registries showed that the current mainstay in the treatment of patients presenting with a CTO is optimal medical therapy (OMT), and only a minority of these individuals receive additional surgical (22–26%) or percutaneous (10–22%) revascularization [3,4]. The general preference for OMT in patients with a CTO originates from the concerns regarding clinical and prognostic patient benefit of revascularization, complexity of CTO percutaneous coronary intervention (PCI) with historically low technical success and high complication rates, high contrast and radiation use, and doubts about the presence of ischemia or viability in the myocardial territory subtended by the occluded artery [5,6]. However, the availability of specialized CTO PCI equipment has been increasingly expanding along with an ongoing progress in percutaneous revascularization techniques and operator expertise [7,8]. This has resulted in enhanced technical success rates from 50–70% to over 90% achieved by high-volume operators [5,8–10]. Therefore, CTO PCI has emerged as a feasible and valuable treatment option warranting new perceptions regarding the traditionally conservative era in CTO treatment. The present review provides an overview of the clinical characteristics and management of patients with a CTO, next to updated perspectives and technical standards in CTO PCI.

2. Clinical presentation of patients with a chronic total occlusion

In general, patients with a CTO are older, more frequently male, and have a relatively unfavorable cardiac risk factor profile as compared with patients with non-occlusive CAD [3,4]. A higher prevalence of diabetes mellitus (34 vs. 26%), hypertension (75 vs. 68%), hyperlipidemia (82 vs. 78%), current smoking (33 vs. 24%), peripheral vascular disease (8 vs. 4%) and prior myocardial infarction (MI) (40% vs. 23%) is observed among patients with a CTO as compared to patients with non-occlusive CAD [3]. This observation illustrates that pronounced CAD, as depicted by a CTO, is accompanied by severe comorbidity.

An undiagnosed or untreated acute thrombotic event is regularly the origin of CTO development, which is supported by electrocardiographic evidence of pathological Q-waves corresponding to the myocardial territory subtended by an occluded artery in a quarter of patients [3]. However, the majority of patients (60%) with a CTO did not suffer from previous MI [3]. In these patients, the occlusion seems to be the result of long-term gradual luminal narrowing allowing for recruitment of collaterals to the occluded vessel. The recruitment of collaterals has a protective role by supplying myocardial blood flow to the CTO territory and thereby preventing acute myocardial ischemia. Preserved viable myocardium subtended by the occluded artery and absence of cardiac symptoms are therefore common observations [11]. The development of a CTO, either after a thrombotic event or by long-term gradual luminal narrowing, is not reserved to the natural vessel wall only and can occur in a previously implanted stent in patients treated with PCI earlier on [12]. Approximately one out of four patients with a CTO does not experience symptoms [13]. Chest pain is a fairly late expression in the ischemic cascade and symptoms can even be absent in the presence of intermittent moderate-to-severe ischemia [14]. The lack of symptoms may be amplified due to autonomic neuropathy in diabetic patients, whom are strongly represented in the CTO patient population [3]. In symptomatic CTO patients, typical cardiac chest pain may be less prominent than shortness of breath or atypical symptoms including physical activity limitation, extensive fatigue, or palpitations due to ventricular arrhythmias [4,6]. Patients with a CTO and an implantable cardioverter defibrillator for primary or secondary prevention of sudden cardiac death have a higher incidence of appropriate delivered therapies and shocks as compared to patients with ischemic cardiomyopathy without a CTO [15]. A CTO in an infarct-related artery (IRA) has been identified as an independent predictor for the occurrence of ventricular arrhythmias, resulting in a two to three-fold higher recurrence rate, even after ventricular tachycardia ablation [15,16]. It could be hypothesized that an IRA-CTO with additional residual ischemia around the necrotic area and the potentially negative influence on long-term remodeling of myocardial scar acts as an initiator for ventricular arrhythmias [15,16].

3. Hazards of chronic total occlusions in patients with an acute coronary event

Chronic total occlusions in a non-IRA are present in 10% of patients presenting with ST elevation myocardial infarction (STEMI) [3]. The presence of a concomitant CTO in patients with STEMI is responsible for a worsened 30-day event rate and long-term prognosis [17]. Prognosis especially deteriorates in case the CTO vessel receives collateral flow from the IRA [18]. This so called “double jeopardy” phenomenon results from an amplified ischemic myocardial territory subtended by the occluded artery due to its dependence on blood flow through the IRA (Fig. 1).

The recently published randomized EXPLORE-trial investigated potential gain in left ventricular function (LVF) due to non-IRA CTO revascularization within one week after the occurrence of STEMI. The hypothesis of this trial was that early CTO revascularization in STEMI patients restores LVF and improves healing of the infarct border zone, yet no additional benefit on LVF was observed in patients with additional CTO PCI compared to OMT alone [19]. Later on a substudy of the EXPLORE-trial demonstrated a greater recovery in regional systolic function in the CTO territory after CTO PCI [20]. However, there is currently insufficient evidence supporting CTO PCI in an acute patient.

4. Benefit of chronic total occlusion revascularization in stable patients

Multiple observational studies have demonstrated the association of successful CTO revascularization with improved clinical outcomes compared to non-successful CTO revascularization. These studies showed in symptomatic patients a significant symptom relief and improved self-reported quality of life and exercise tolerance [21–23]. Successful CTO revascularization significantly reduces myocardial ischemic burden (Fig. 2) and a modest positive effect on LVF and left ventricular remodeling has been suggested [24–27]. Furthermore, successful CTO PCI has been associated with a reduced need for coronary artery bypass graft surgery (CABG), and may provide a long-term survival benefit compared to non-successful revascularization [21,24]. The beneficial effect of successful CTO PCI on long-term survival is, despite more major comorbidities, maintained in the elderly (≥75 years) [28]. Importantly, the observational nature of the aforementioned studies cannot exclude the impact of confounding and selection bias on clinical outcomes. Recently, the results from the DECISION-CTO trial (NCT01078051) and the EURO-CTO trial, as the first randomized studies to elucidate the surplus clinical value of CTO PCI over OMT alone in terms of health status and safety outcomes, were revealed (Table 1) [29]. In the DECISION-CTO trial, the three-year rate of the composite endpoint of all-cause death, MI, stroke, and any revascularization in the intention-to-treat analysis was similar between the PCI and OMT groups (20.6% vs. 19.6%) [30, abstract only]. It remains challenging to draw definite conclusions within this trial due to delayed and incomplete recruitment

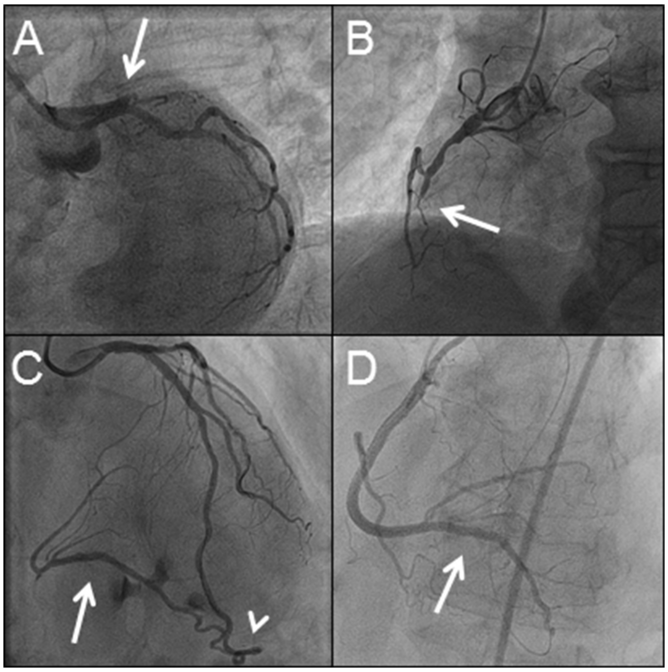

Fig. 1. The risk of a non-IRA CTO in a patient with ACS. A STEMI patient with an acute thrombotic occlusion (arrow) of the proximal LAD (A) and a CTO RCA (arrow: proximal cap) (B). After primary PCI of the LAD a very well-developed collateral over the apex (arrowhead) appeared to be the predominant source of collateral flow to the CTO territory (arrow) (C). After successful recanalization of the CTO RCA in a second procedure (D), antegrade flow to the CTO territory (arrow) eliminated dependency on the donor artery. ACS, acute coronary syndrome; CTO, chronic coronary total occlusion; IRA, infarct-related artery; LAD, left anterior descending artery; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST elevation myocardial infarction.

of patients, the revascularization of other non-occlusive lesions in addition to CTO PCI after randomization and baseline health status assessment, the high crossover rate to the PCI group (15–20%), and inclusion of periprocedural MI in the primary outcome. Interim analysis of the EURO-CTO trial revealed a significantly improved one-year health status in the PCI group compared to the OMT alone arm, while the major adverse cardiovascular events rate was comparable [29]. Study completion including the results of the three-year composite endpoint of all-cause death and non-fatal MI is expected in 2018. The SHINE-CTO trial (NCT02784418) is designed to determine whether CTO PCI improves patients' symptoms by randomizing to CTO PCI or a sham procedure. The results of the SHINE-CTO trial are expected to be available in 2018. Although these first trials pave the way toward appropriate treatment decision-making for stable patients with a CTO, more well-designed randomized trials will be needed to provide the necessary evidence to guide treatment.

5. Diagnostic work-up

Once the diagnosis of a CTO in a patient is established, the indication for revascularization of a CTO can be determined similar to CAD in general, by the presence of symptoms and/or the extent of ischemia and viability (Fig. 3) [31]. Normal wall motions or hypokinesia of the myocardium subtended by the occluded artery per definition excludes non-viability. In the presence of myocardial viability, CTO revascularization is considered beneficial if there are persisting invalidating symptoms despite OMT [31,32]. According to the European guidelines, CTO revascularization is also indicated if myocardial ischemia comprises >10% of the left ventricle irrespective of symptoms [31]. The latter is based on observational studies that hint toward a prognostic benefit of revascularization in the presence of CAD in general (not CTO specific) and a large ischemic burden [33]. Randomized trials are lacking to support this hypothesis although the ongoing ISCHEMIA trial (NCT01471522) is addressing this issue. The American guidelines include additional clinical and angiographic characteristics to determine the appropriate use of myocardial revascularization in asymptomatic patients, including CTO lesions [32]. In case of one- or two-vessel disease and intermediate- or high-risk findings on (non)invasive testing, revascularization may be appropriate, and in a few subsets of these asymptomatic patients revascularization can be considered appropriate when there is proximal LAD or left dominant left circumflex involvement [32]. In asymptomatic patients with three-vessel disease and low-risk findings on noninvasive testing, revascularization in general may be appropriate, and can be considered appropriate in some cases in the presence of diabetes and intermediate or high anatomical disease complexity. In asymptomatic patients with three-vessel disease and intermediate- or high-risk findings on noninvasive testing, revascularization (preferably CABG) is considered appropriate regardless of anatomical disease complexity [32].

Angiographically well-developed collaterals to the occluded artery are often assumed to be sufficient to prevent ischemia. Non-invasive and invasive studies have clearly demonstrated the limited functional capacity of collaterals to provide sufficient myocardial perfusion in the vast majority of patients (Fig. 4) [14,34]. Therefore, the existence of well-developed collaterals should not guide the indication for revascularization. Marked ischemia holds prognostic relevance, while a significant benefit in ischemia reduction can be established with CTO PCI [25,35]. In case of significant wall motion abnormalities of the myocardium subtended by the occluded artery, the diagnostic work-up should be primarily focused on the detection of myocardial viability. Without signs of myocardial viability, no recovery of LVF can be anticipated and CTO revascularization is considered inappropriate [25,26]. Conversely, the presence of substantial myocardial viability prior to revascularization is a predictor for improvement of regional and global LVF [25,26]. Myocardial ischemia and viability can be assessed using an array of non-invasive imaging tests [36]. The choice of non-invasive imaging for CTO patients should be based on local availability and expertise.

6. New considerations concerning CTO PCI as choice of treatment

While CTOs are diagnosed in 16–18.4% of patients with CAD, a national report stated that CTO PCI represented only 4.8% of the total PCI volume in 2013 in the United States [3–5]. In addition, national reports from the Swedish Coronary Angiography and Angioplasty Registry (average in 2005–2012), the United Kingdom (in 2012) and a Japanese multicenter registry (average of all elective procedures in 2008–2013) reported that CTO PCI comprised 5.8%, 5% and 10.1% of the total PCI volume, respectively [4,37,38]. CTO PCI has traditionally been considered as a less appropriate treatment strategy relative to non-CTO PCI and surgical revascularization, and OMT is currently the most frequently applied treatment option [3,4,6]. In every patient with a CTO, especially in the presence of multivessel disease, the international guidelines advocate an individualized risk-benefit analysis by the Heart team encompassing clinical and angiographic considerations to guide treatment decision making [31,32,39]. A recent analysis showed that incomplete revascularization following CTO PCI has a detrimental effect on long-term clinical outcomes [40]. The SYNTAX II study demonstrated in addition the incremental value of several new developments in the field of complex PCI in patients with triple-vessel disease, leading to improved clinical outcomes compared to the PCI performed in similar patients in the original SYNTAX-I trial [41,42]. Of note, the implementation of contemporary revascularization techniques in CTO PCI by experienced operators led to a 87% success rate that was achieved overall in 22 participating centers [41]. These technical developments and increasing success rates in CTO PCI leading to complete revascularization should play a role in the interpretation of current rather conservative recommendations for percutaneous CTO revascularization [8,31]. Randomized trials are warranted to be able to accurately appreciate the

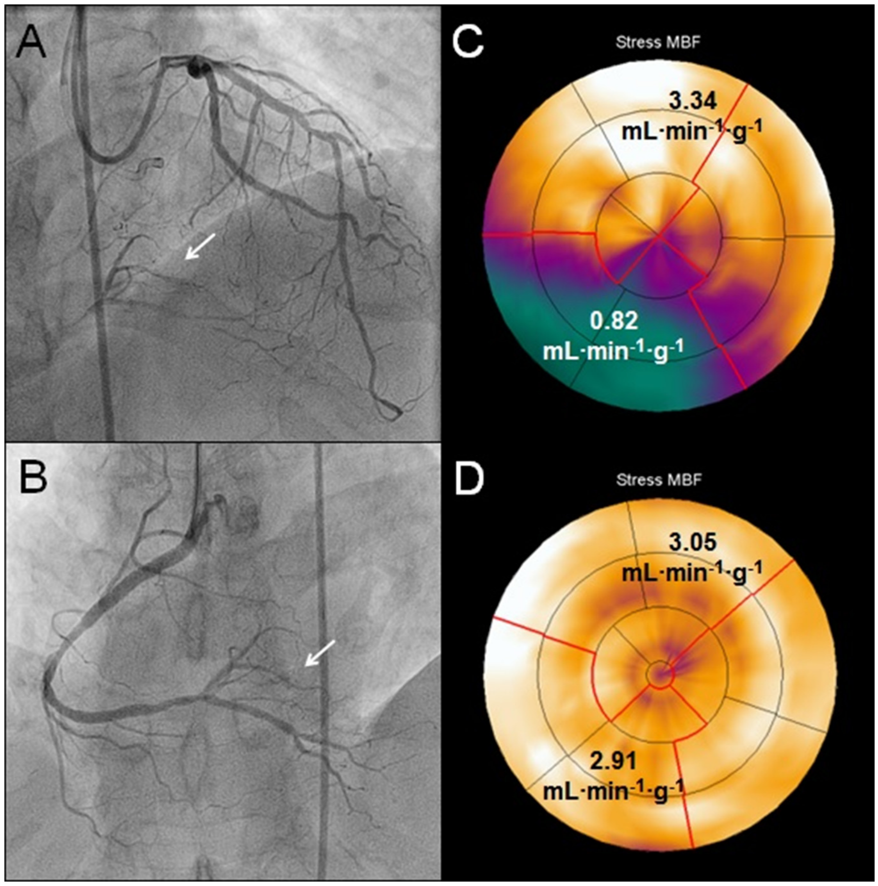

Fig. 2. Myocardial ischemia induced by a CTO RCA and recovery of myocardial perfusion after successful PCI. The distal vascular bed of the RCA (white arrow) prior to PCI receives collateral flow through septal and epicardial collaterals from the LAD and LCX respectively. (A) Re-established antegrade flow to the distal vascular bed of the RCA (white arrow) after CTO PCI (B). PET perfusion shows myocardial ischemia (C) with recovery after revascularization (D). LCX, left circumflex artery; PET, positron emission tomography. Other abbreviations as in Fig. 1.

potential advances of these developments in CTO PCI. In 2012, a hybrid percutaneous treatment algorithm focusing on percutaneous CTO revascularization in a most safe, effective, and efficient manner was introduced [7]. Current standards and considerations within the framework of this so called "hybrid approach" in CTO PCI will be further discussed.

7. Percutaneous revascularization of chronic total occlusions: preparation is key

Once a clinical indication for CTO PCI has been established, planning and preparation of the procedure will be a major factor for

Table 1
Three randomized trials concerning the additional clinical value of CTO PCI over OMT alone.

	DECISION-CTO trial	EURO-CTO trial	SHINE-CTO trial
Design	PCI + OMT vs. OMT only	PCI + OMT vs. OMT only	PCI vs. sham procedure
Estimated patients	1284	1200	142
Recruited patients	834 (enrollment stopped)	407 (enrollment stopped)	Ongoing
Major inclusion & exclusion criteria	CTO in a major artery ≥2.5 mm Stable angina, ACS or ischemia Non-CTO PCI before randomization No LVEF <30%	CTO in a major artery ≥2.5 mm Symptoms/ischemia and viability Non-CTO PCI before randomization No previous MI <1 month	Clinically-indicated CTO PCI Symptoms related to the CTO Already treated with OMT No previous MI <7 days
Primary endpoint(s)	Three year composite of - Death from any cause - MI - Stroke - Any revascularization	1) Health status at 1 year - SAQ 2) Three year composite of: - All-cause death - Non-fatal MI	Health status at 1 month - SAQ
Primary results [29,30 (abstract only)]	PCI + OMT 20.6% vs. OMT only 19.6% ($p = 0.54$) OMT non-inferior to PCI + OMT in intention-to-treat analysis OMT not non-inferior to PCI + OMT in per-protocol and as-treated analyses	1) More improvement after PCI in: - Quality of life - Anginal frequency Equal between groups: - Physical limitation - Anginal stability - Treatment satisfaction 2) Results are awaited	Results are awaited

ACS, acute coronary syndrome; CTO, chronic coronary total occlusion; LVEF, left ventricular ejection fraction; MI, myocardial infarction; OMT, optimal medical therapy; PCI, percutaneous coronary intervention; SAQ, Seattle Angina Questionnaire.

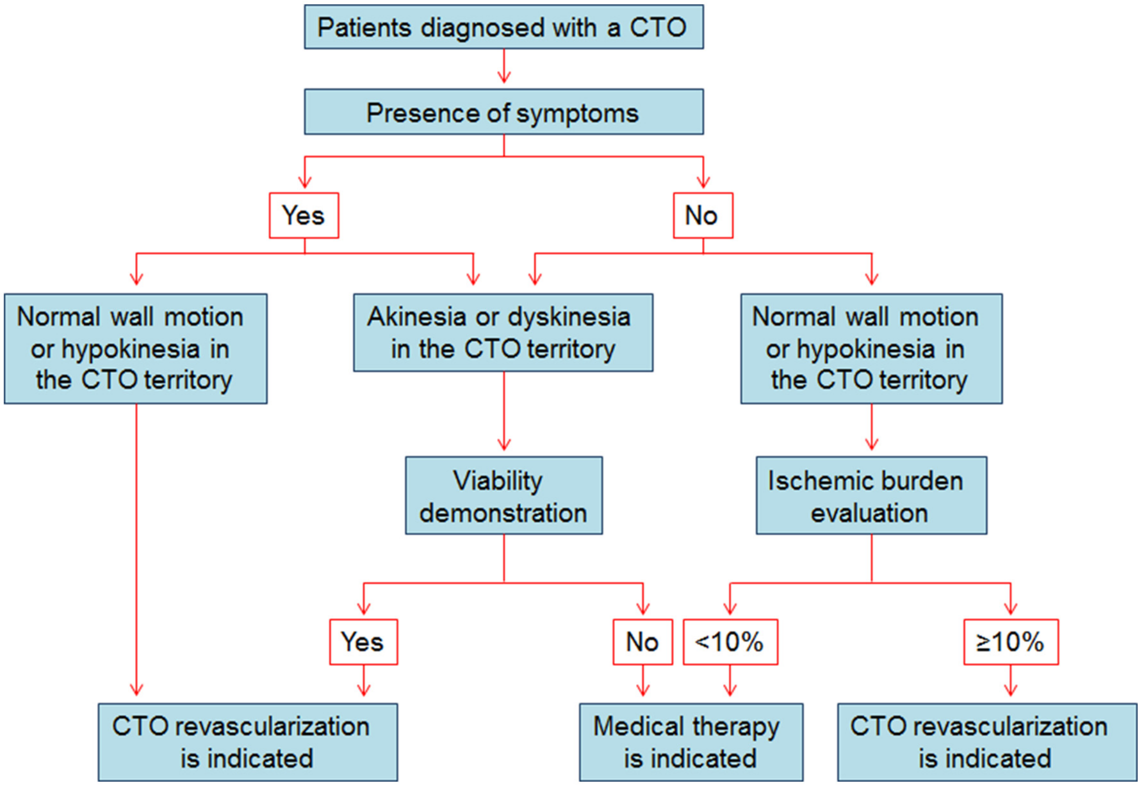

Fig. 3. Diagnostic and treatment algorithm in patients presenting with a chronic coronary total occlusion.

revascularization success. Double arterial access is strongly recommended since it facilitates dual contrast injection and a potential retrograde approach [43]. Such access can be femoral-radial, bifemoral, or biradial. The latter however is limited by use of ≤7 French guiding catheters. An 8-French guiding catheter for the CTO vessel enables the utilization of the full range of dedicated CTO PCI materials and is preferred in complex CTO PCI cases over ≤7 French guiding catheters only [44]. In general, more aggressive support guiding catheters are preferred to provide the required penetrative power to deal with the often resilient proximal cap and adequate support to maneuver a microcatheter through the retrograde channel. However, access site and guiding catheter selection always depends on patient and angiographic suitability as well as the preference of the CTO operator [43].

Careful assessment of the target CTO lesion and other angiographic characteristics is essential for adequate procedural planning. It is recommended to start virtually all CTO procedures with dual contrast

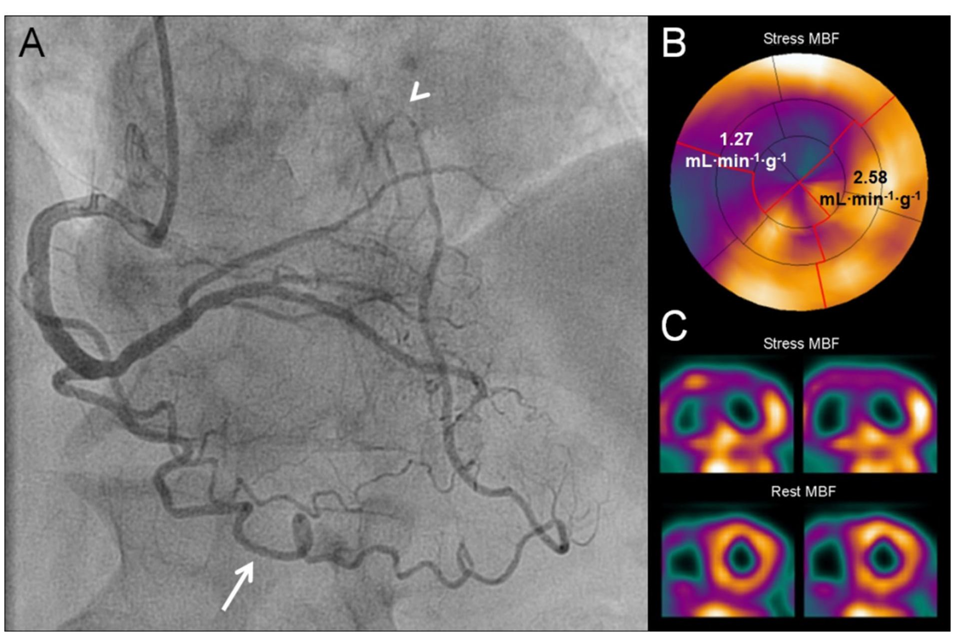

Fig. 4. Extensive myocardial ischemia despite angiographically well-developed collaterals. A Epicardial (arrow) and septal collaterals supplying retrograde flow to the distal vascular bed of a CTO in the proximal LAD (arrowhead). PET perfusion shows extensive myocardial ischemia in the LAD territory despite the angiographically well-developed collaterals (B and C). Abbreviations as in Figs. 1 and 2.

injection, with the exception of sole ipsilateral collaterals, as it ensures optimal visualization of the CTO body and collateral filling. Dual injection is performed by contrast injection in the donor vessel followed by a slightly delayed simultaneous injection in the CTO vessel. Prolonged image acquisition at low magnification without table panning from multiple angles allows adequate appreciation of the angiographic information needed to determine an adequate treatment strategy.

In the hybrid approach, four angiographic characteristics (Fig. 5) guide initial strategy selection (Table 2) [7]:

1) The proximal cap: location and morphology. Proximal cap morphology is distributed over three classifications with increasing difficulty to approach: tapered, blunt, or ambiguous. Proximal cap ambiguity indicates the inability to define its location and can be due to the origin of a side-branch near the proximal cap.
2) CTO lesion length. Based on the Japanese CTO registry, a cut-off of 20 mm is used to dichotomize with <20 mm more suitable for a wire escalation technique and ≥20 mm for a dissection and reentry technique as initial approach [7,45]. Noteworthy, lesion length does not guide preference for an antegrade or retrograde approach.
3) Distal landing zone. The distal landing zone refers to the part of the CTO vessel beyond the occlusion. Evaluation of the distal landing zone includes vessel size, angiographic health, and its presence near a bifurcation or side branch. A proper distal landing zone would favor an antegrade (dissection and re-entry) approach, whereas in case of a poor distal target an initial retrograde approach may be more suitable.
4) The interventional suitability of collaterals. Favorable aspects of an interventional collateral are a suitable angle to engage the collateral from the donor vessel, minimal tortuosity, a visible

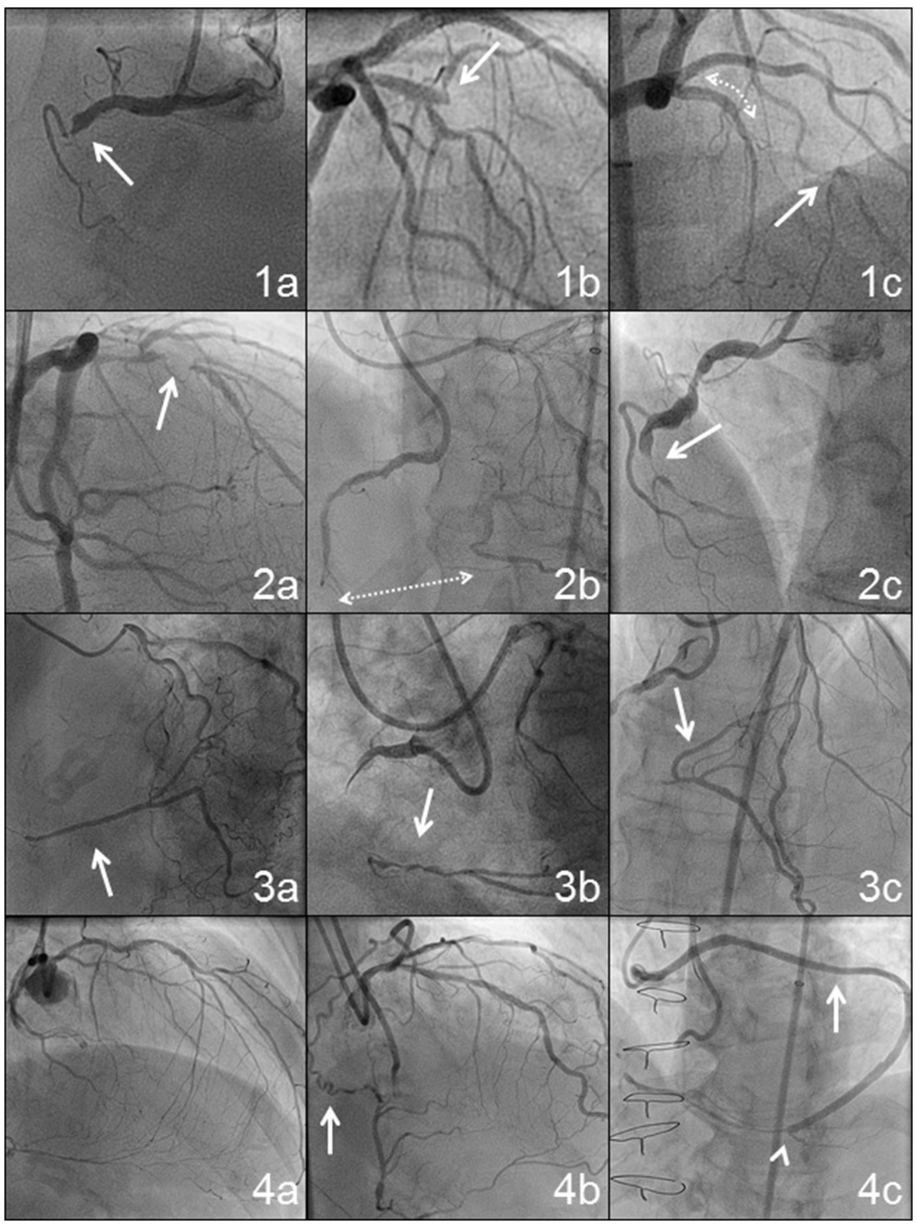

Fig. 5. Examples of the four main angiographic characteristics guiding strategical planning in CTO PCI. 1a CTO RCA with a tapered proximal cap, 1b CTO LAD with a blunt proximal cap, 1c CTO LAD with an ambiguous proximal cap (tapered line), the distal cap is also shown (arrow), 2a CTO LAD with a short lesion length (<20 mm), 2b CTO RCA with a long lesion length (>20 mm), 2c a functional CTO RCA with TIMI grade flow I, 3a CTO RCA with a good distal landing zone, 3b CTO RCA with a diseased distal landing zone, 3c CTO RCA with significant side branches near the distal cap, 4a CTO RCA and multiple potentially interventional septal collaterals, 4b CTO RCA and a potentially interventional epicardial collateral arising from the LCX, 4c CTO RCA and a vein graft (arrow) with an anastomosis to the distal RCA (arrowhead) serving as a potential retrograde pathway. TIMI, thrombolysis in myocardial infarction. Other abbreviations as in Figs. 1 and 2.

Table 2
Favorable angiographic characteristics for each of the percutaneous revascularization techniques in CTO PCI.

	AWE	ADR	RWE	RDR
Clear proximal cap	+	+	−	−
Lesion length ≥20 mm	−	+	−	+
Good distal landing zone	+	+	−	−
Interventional collaterals	−	−	+	+

ADR, antegrade dissection and reentry; AWE, antegrade wire escalation; CTO, chronic coronary total occlusion; PCI, percutaneous coronary intervention; RDR, retrograde dissection and reentry; RWE, retrograde wire escalation.

connection, and an adequate entry of sufficient length to penetrate the distal body of the CTO. The presence of multiple collaterals to the CTO vessel reduces the risk of intra-procedural ischemia due to mechanical obstruction during collateral engagement with a microcatheter. All potential retrograde pathways, including septal and epicardial collaterals and (occluded) bypass grafts, should be evaluated for interventional suitability.

8. Antegrade wire escalation

Favorable angiographic findings for antegrade wire escalation (AWE) are: an unambiguous (preferably tapered) proximal cap, <20 mm occlusion length, and a good distal target. In AWE (Fig. 6), usually the initial wire choice is a (non-traumatic) polymer-jacketed wire with low-gram tip load (≤1 g) for loose tissue tracking. Penetration force and maneuverability of the wire can be supported by advancing a microcatheter near to the tip. With lack of progress, stepwise escalation to wires with increasing tip-load should be used until successful CTO crossing is achieved or strategy is altered (vide infra for other strategies). The subsequent wire in AWE is determined by lesion characteristics. In unclear, long or tortuous pathways, a non-tapered polymer-jacketed wire with moderately high-gram tip load is preferred, while in case of a short and clear path and target a stiff tapered wire with high-gram tip load will be more efficient for direct penetration of tissue.

The Japanese CTO score (J-CTO score) can be applied when considering AWE. The J-CTO score is an angiographic model predicting the probability of successful CTO crossing within 30 min performing AWE only, using 5 independent predictors for failure [45]. A previous failed attempt, a blunt proximal cap, presence of any calcification, >45° bending within the CTO segment, and ≥20 mm occlusion length each adds 1 point to the J-CTO score. With every increase in J-CTO score the probability of successful AWE within 30 min decreases [45]. While maintaining its predictive value for complexity of CTO recanalization, the J-CTO has limited value in predicting final success rate in case of an experienced operator using the hybrid approach (including antegrade dissection and reentry (ADR) and retrograde techniques) [9].

9. Retrograde techniques

Retrograde approaches are complementary techniques to AWE and have allowed for a significant increase in technical success rates [46,47]. Generally retrograde approaches result in longer procedural times and higher radiation and contrast requirements [46]. However, they are often used for CTO lesions of higher anatomic complexity and are regularly the key to successful CTO crossing after a failed antegrade approach [46,47]. Periprocedural complications occur more frequently in retrograde approaches compared to antegrade approaches, mainly because of the higher occurrence of periprocedural MI and the possibility of donor vessel- or collateral injury [46,48]. A retrograde approach may be favorable over an antegrade approach in case there is an ostial or ambiguous proximal cap or a poor distal landing zone, and a suitable interventional collateral. Crossing an available bypass graft in post-CABG patients is safe and generally successful [49]. Septal collaterals are also commonly suitable and safe pathways to reach the CTO vessel [46,47,49]. A major advantage of the septal collateral is its tolerability for channel perforations, as it practically never leads to cardiac tamponade since the perforation would leak to one of the ventricular cavities or results in a (usually) self-limiting intraseptal hematoma. Successful septal crossing depends predominantly on tortuosity rather than size, and septal collaterals can be crossed using a tip injection facilitated or blind septal surfing technique [50]. The tip injection technique includes sequential distal microcatheter tip injections within the septal collateral in order to visualize a distal connection to the occluded artery. Septal surfing involves probing of septal channels by trial and error in a more blinded fashion in search of a path of low resistance. By using this technique, visualization of septal channels on the coronary angiogram is of less importance. The course of an epicardial collateral can be contralateral or ipsilateral including bridging collaterals. Epicardial collateral crossing is associated with a higher incidence of non-Q-wave MI and channel injury requiring treatment as compared with septal collaterals and is therefore more challenging [49]. Over-the-wire balloons are contraindicated in epicardial collaterals due to the risk of epicardial channel injury. Dedicated low-profile microcatheters allow a more safe and effective crossing of these collaterals [51].

Most operators report that the distal cap is easier to cross compared to the proximal cap [52]. The occlusion can be crossed using the retrograde wire escalation (RWE) technique, similar to AWE. If the guidewire enters the subintimal space or CTO characteristics are unfavorable for RWE, a retrograde dissection and reentry (RDR) technique can be initiated. In RDR, a guidewire will be navigated into the subintimal space distal or within the occlusion to cross the CTO through the subintimal space. The most common used RDR technique is the reverse controlled antegrade and retrograde subintimal tracking (CART) technique [46,51]. In this technique adjacent subintimal dissection planes around or proximal to the CTO are created with an antegrade as well as a retrograde guidewire. Of paramount importance before applying reentry into the vessel lumen is the determination of a proper reentry zone.

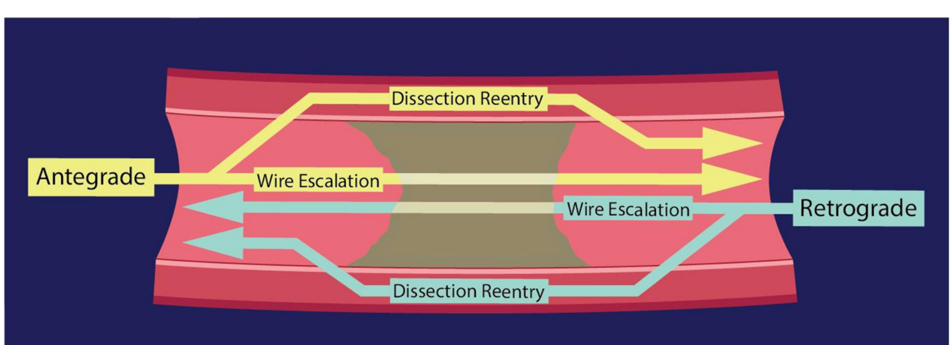

Fig. 6. The four strategies applied in CTO PCI according to the hybrid approach.

Subintimal passing of bridging collaterals and side branches can lead to their loss after coronary angioplasty, which can potentially result in MI. In reverse CART, a connection between both subintimal spaces is created by inflating a balloon over the antegrade guidewire. Subsequently, the retrograde guidewire passes through the subintimal track created by the antegrade guidewire before making reentry into the vessel true lumen [7]. Once successful retrograde crossing of a CTO is realized, the final step should be wire externalization. After the retrograde guidewire and microcatheter have been directed into the antegrade guiding catheter, the retrograde wire can be changed for an externalization guidewire (>3.30 m), which can be advanced until it exits the Y-connector of the antegrade guiding catheter. This wire externalization technique creates a closed system enabling antegrade coronary angioplasty. The crossed collateral endures high forces while maintaining this externalized wire and should be protected by the retrograde microcatheter at all times. If the conventional externalization method does not succeed, snaring the wire, the tip-in technique and the rendezvous technique offer an alternative to succeed the retrograde approach. In snaring, the antegrade guiding catheter should be pulled back, and subsequently the retrograde externalization wire has to be directed into the aorta through one of the loops of the antegrade snare. Once the externalization wire has been “snared”, it will be pulled back into the antegrade guiding catheter to allow for externalization [52]. The tip-in technique involves the advancement of an antegrade microcatheter over a retrograde wire, and can usually be accomplished in the aortic arch, where the retrograde wire and antegrade microcatheter can meet in the outer curve of the antegrade guiding catheter [53]. Once the tip-in technique has been successful, the antegrade microcatheter can be advanced over the retrograde wire to the distal vessel, allowing for antegrade coronary angioplasty. The tip-in technique shows similarities with the rendezvous technique, that uses the alignment of an antegrade and retrograde microcatheter to direct the antegrade wire into the retrograde microcatheter. After progressing the antegrade wire through the retrograde microcatheter further down beyond the occlusion, the operator can proceed with antegrade coronary angioplasty [54].

10. Antegrade dissection and reentry

The ADR technique is the subintimal passage of a CTO in an antegrade fashion with reentry into the distal vessel lumen [8]. This technique is especially useful for crossing of long lesions (≥20 mm) with a clear proximal cap and a good distal landing zone. ADR should be considered complementary to other techniques enabling higher procedural success rates and, several studies reported comparable complication rates after the use of ADR and intraplaque crossing techniques [55–57]. Subintimal tracking can be achieved with the knuckle wire technique or device-assisted using a CrossBoss catheter (Boston Scientific, Maple Grove, MN, USA). The knuckle technique is used to achieve blunt cleavage of the subintimal space across the CTO by pushing a looped polymer-jacketed wire (“the knuckle”) toward the distal landing zone. The CrossBoss catheter is an over-the-wire catheter and its blunt, low-profile tip minimizes vessel trauma during subintimal tracking and preserves relatively more side-branches. Due to its higher crossing profile, the CrossBoss catheter also allows in some patients for effective intraplaque crossing, especially in case of in-stent CTOs [12]. The first introduced reentry technique was the wire-based subintimal tracking and reentry (STAR) technique in which a forward push of the knuckle results in spontaneously reentry to the vessel lumen [8]. The wire-based limited antegrade subintimal tracking (LAST) technique uses a straight-tip guidewire with high tip load for reentry. LAST preserves relatively more side branches and has a higher success rate compared to the STAR-technique [58]. An alternative for these wire-based reentry techniques is the Stingray Balloon Catheter

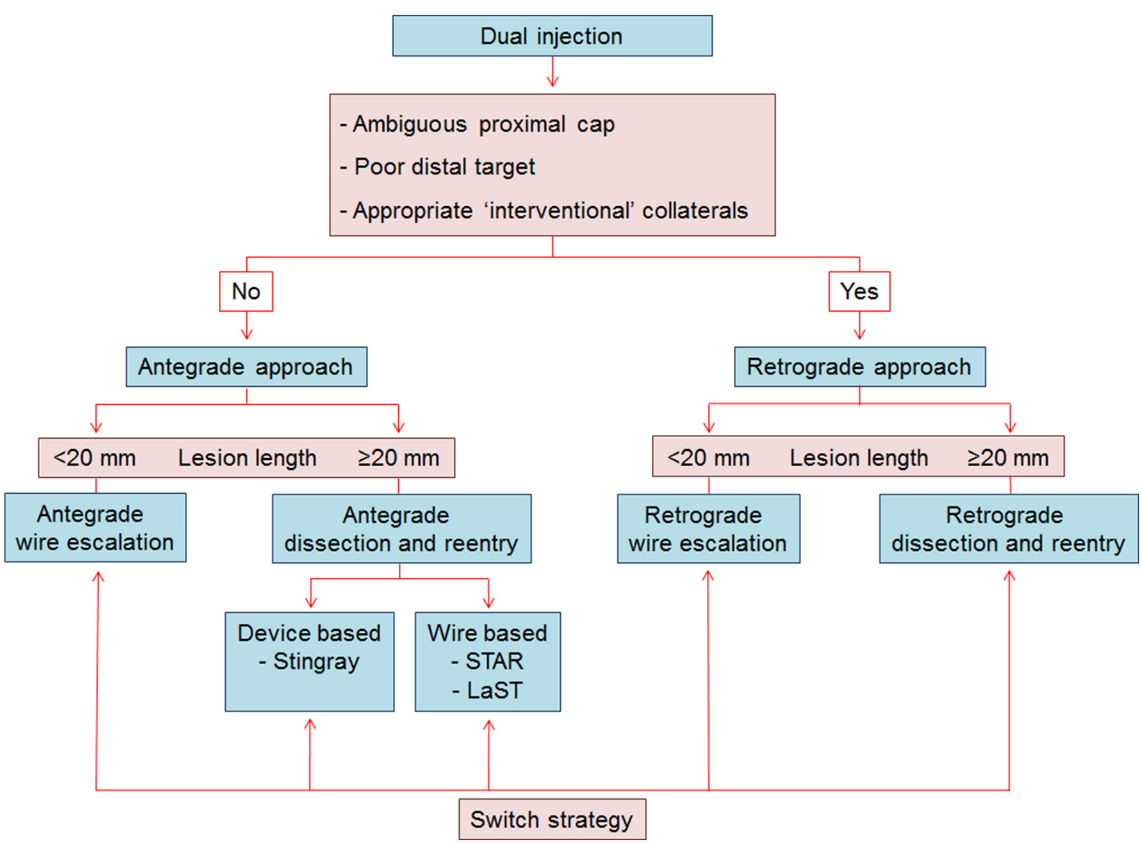

Fig. 7. The hybrid algorithm for crossing CTOs, dictated by anatomical features of a CTO in a native coronary artery. LAST, limited antegrade subintimal tracking; STAR, subintimal tracking and reentry.

(Boston Scientific, Maple Grove, MN, USA), designed to deploy in the subintimal space. The exit ports on either side of the balloon can be selectively engaged to provide reentry in the vessel lumen [59]. The CrossBoss/Stingray combination facilitates a more controlled dissection plane as well as reentry compared to the LAST- and STAR-techniques with relatively high success rates and improved long-term clinical outcomes [58].

11. The hybrid approach

The hybrid algorithm provides a consistent and reproducible format enabling flexible change to other techniques when one fails (Fig. 7). The PROGRESS CTO score and the RECHARGE score are 2 novel easy-to-use predictive tools to assess the risk for technical failure in CTO PCI. Both scores are based on the presence or absence of several CTO-related angiographic characteristics and are validated in a cohort of hybrid approach based CTO PCI [60,61]. Previous studies indicated more complications in CTO PCI compared to non-CTO PCI including a higher rate of major adverse cardiac events and perforations along with higher contrast- and radiation use (with the potential for radiation-related dermal injury and contrast-induced renal dysfunction) [5,62]. Failed attempts to open a CTO compared to successful CTO procedures are associated with a higher incidence of periprocedural complications [63]. On the contrary, the application of the hybrid approach in high-volume CTO PCI centers has led to technical and procedural success rates up to 90–95% with acceptable periprocedural complication rates [8–10]. A recent European multicenter study including 17 high and lower experienced CTO PCI centers using the hybrid approach showed an overall low complication rate [8]. Of note, the abovementioned proposed techniques and considerations within the framework of the hybrid approach apply for trained hybrid CTO operators only. Before using the hybrid algorithm in CTO PCI, the CTO operator needs to be familiar with the full range of techniques and dedicated CTO equipment. Experience with a variety of tools to deal with the potential acute periprocedural complications, such as perforations or tamponade requiring pericardiocentesis is necessary. PCI operators whom have no experience with the technical standards used in the hybrid approach could master the antegrade true-to-true approach for less complex CTO lesions such as the lesions with a J-CTO score of 0 or 1, however, should refer cases of higher anatomic complexity to more experienced CTO centers [64]. It is advised for starting CTO operators to attend to CTO focused meetings and to be assisted by more experienced operators through a proper proctorship to develop stepwise the dedicated skills for performing CTO PCI.

12. Current perspectives

CTOs are commonly diagnosed in patients with CAD and have a negative impact on quality of life and long-term prognosis. Observational studies point toward additional benefits of CTO PCI over OMT alone, however, randomized clinical trials with hard outcomes are eagerly awaited for further exploration. With nowadays high success and acceptable complication rates, patient selection for percutaneous revascularization should be focused on anticipated patient benefits instead of coronary anatomic complexity. With judicious patient selection and a dedicated operator with the appropriate expertise, CTO PCI has become an important tool in our armamentarium for coronary revascularization.

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