Chapter 4

Chronic Total Occlusion (CTO): Scientific Benefit and Principal Interventional Approach

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Abstract

Chronic total occlusion (CTO) of coronary arteries are found in about 20% of patients undergoing percutaneous coronary intervention (PCI) and in about 50% of post-CABG patients. Specialized centers can now achieve success rates of over 85%, which is a result of technical advancements in retrograde techniques irrespective of the CTO anatomy. Due to the complexity of retrograde CTO-techniques, a consensus paper issued by the EuroCTO-Club requires interventional cardiologists to have sufficient experience in antegrade approaches (>300 antegrade CTO-cases, 50/year) with additional retrograde training (25 retrograde cases each as first and second operator) before becoming an independent retrograde operator. The increased investment in time and technical resources may only be justified if the patient has a clear clinical benefit. However, technical advancements and the clearer evidence that complete revascularization can be achieved in patients with coronary multivessel disease have attracted growing interest in recent years from interventional cardiologists in treating CTO. The chapter will review current knowledge in the interventional treatment of CTO and focuses on indications and the potential benefits for the individual patient being based on the current state of scientific evidence.

Keywords: chronic total occlusion, CTO, percutaneous coronary intervention, PCI

1. Introduction

Chronic total occlusions (CTO) of coronary arteries are defined as a complete coronary arterial occlusion (thrombolysis in myocardial infarction, TIMI grade 0) being present for more than 3 months. About 20% of patients undergoing percutaneous coronary interventions (PCI) reveal a CTO, whereas in patients with prior coronary artery bypass grafting (CABG), CTOs are even more common in more than 50% [1]. Although registry data demonstrate an improvement of the patients' symptoms such as angina pectoris or dyspnea [2] and a reduction of adverse cardiac events [3, 4] after successful revascularization of a CTO, the overall clinical benefit is still under controversial debate, since prospective randomized controlled studies are still lacking [5, 6]. This is due partly to the greater complexity of catheter-based interventional techniques and the higher demand for materials compared to PCIs of nonchronically occlusive coronary lesions. In contrast, over the last decade, modern and novel developments of special techniques and materials increased the success rates of CTO revascularization in specialized centers toward more than 85% alongside acceptable low complication rates. This technical advance and the growing scientific evidence envisaging potential complete coronary revascularization in patients suffering from coronary multivessel disease [7, 8] have pushed CTO-PCIs into the spotlight of modern interventional cardiology.

2. Indication to revascularize a CTO

In more than 50% left ventricular (LV) function is still preserved in the territory of supply of the CTO artery [9], whereas the maintaining supply by collateral connections (CCs) is sufficient for only 20% of CTO patients while preventing exercise-induced myocardial ischemia [10, 11]. The fractional flow reserve (FFR) distally of the CTO lesion is usually less than 0.5 reflecting an insufficient collateral circulation [12]. Accordingly, exercise-testing oftentimes reveals an exercise-induced myocardial ischemia in the territory of supply of the chronically occluded coronary artery.

No prospective randomized controlled studies have been published yet evaluating clinical endpoints in patients with CTO-PCI compared to patients being treated conservatively by optimal medical therapy. However, there are numerous observational studies comparing a successful with unsuccessful CTO-PCI. A meta-analysis of these retrospective registry data show an improvement of angina pectoris and a decrease of consecutive need for CABG surgery after successful CTO-PCI [2].

Although symptoms' relief instead of prognostic benefit represents the primary indication for an elective CTO-PCI, the prognostic aspect is debated increasingly as a potential indication. Accordingly, there are still only retrospective cohort studies available suggesting a potential prognostic benefit after successful CTO-PCI [13]. The largest CTO registry from the UK database demonstrated a 30% improvement of long-term survival both for patients with successful PCI of at least one CTO as well as for those with complete coronary revascularization in 13,433 CTO patients [14].

Sub-analyses of the New York State Registry including more than 21,000 patients with elective coronary stent implantation showed that a complete revascularization was associated with an improved adjusted long-term survival compared to incomplete revascularization including CTOs [8]. These data support the concept targeting the complete revascularization including the revascularization of coronary CTOs.

Figure 1 shows own data from a recent monocentric analysis including 1,642 CTO-patients. The prognostic benefit of a CTO-PCI depends on the extend of coronary artery disease and is most prominent in patients with a coronary three-vessel disease [15].

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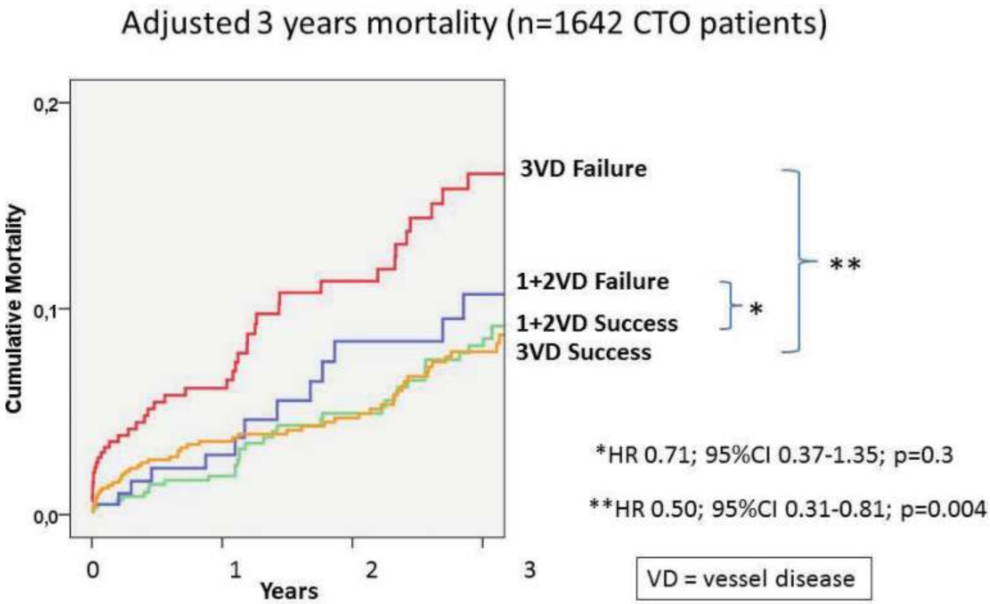

Figure 1. Adjusted 3-year mortality of 1,642 CTO patients presenting at the University Heart Centre Bad Krozingen, Germany. A clear prognostic benefit is shown for complete coronary revascularization, especially in patients with a coronary three-vessel disease including a CTO (HR, hazard ratio; CI, confidence interval) a CTO (HR, hazard ratio; CI, confidence interval) [15].

A main mechanism for a beneficial prognostic influence of a successful CTO-PCI may consist in an improved tolerance for future acute coronary syndromes. A sub-analysis from the HORIZONS-AMI-study showed that patients with an ST segment elevation myocardial infarction (STEMI) and a concomitant CTO revealed a significantly increased mortality both in the acute phase and within long-term follow-up, especially in the presence of a coronary three-vessel disease [16]. Another registry database demonstrated that the presence of a CTO was associated with the future development of malignant ventricular arrhythmias in patients with an ischemia-related LV dysfunction [17].

The so-called EURO-CTO-study has just finished the recruiting phase. It represents the first prospective and randomized CTO-study comparing CTO-PCIs with optimal medical treatment focusing on the improvement of predefined clinical endpoints (i.e., quality of live at 1 year, death or myocardial infarction at 3 years). Furthermore, the prospective DECISION-PCI-study from Korea randomizes CTO patients either to PCI or optimal medical treatment in order to evaluate the influence of CTO-PCI on cardiovascular mortality and future myocardial infarction at 5 years.

Whether LV function being assessed by cardiovascular magnetic resonance imaging (cMRI) might be improved is currently being evaluated within the REVASC-study, in which 200 patients with CTOs are randomized to PCI or optimal medical treatment. Within a prior smaller cMRI study, regional LV function depended on the extend of transmural scarring after myocardial infarction [18], whereas a further meta-analysis of registry data demonstrated an improvement of global LV ejection fraction (LVEF) of 4.7% [19].

3. Principal approaches during CTO-PCI

As shown in **Figure 2**, the principal factors on which the indication for revascularization of a CTO depends on comprise the following:

- Extend of patient's symptoms under optimal medical therapy.
- Exercise testing.
- Global and regional ventricular function and viability.
- Severity of coronary artery disease.
- Localization and morphology of the CTO.

Considering these factors before CTO-PCI allows the estimation of the potential benefit for the patient, as well as the technical severity and risk being associated with the intervention. Using the so-called J-CTO-score reveals optimal graduation of the complexity of the CTO-lesion itself and is more commonly being applied by experienced CTO operators [20].

The latest European guidelines for myocardial revascularization from the year 2014 [21] recommended a class IIa, with a level of evidence B ("*Percutaneous recanalization of CTOs may be considered in patients with suspected ischemia reduction in a corresponding myocardial territory and/or angina relief.*"), and retrograde recanalization techniques are recommended only by a class IIB, level of evidence C ("*Retrograde recanalization of CTOs may be considered after a failed antegrade approach or as the primary approach for selected patients.*").

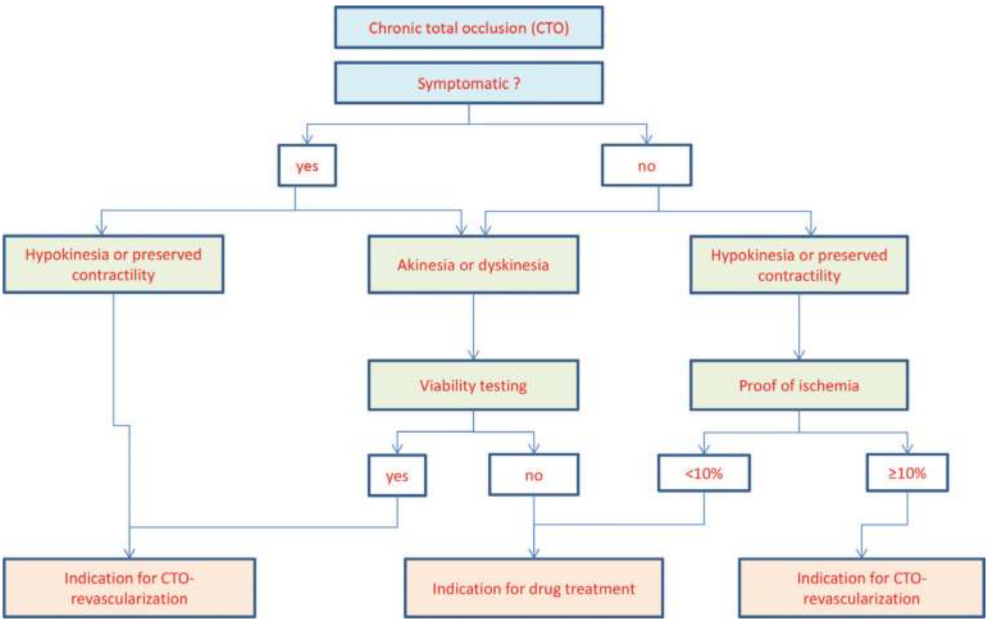

Figure 2. Indications for CTO-revascularization.

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This lower recommendation class compared to the PCI of nonchronically occluded coronary lesions is in conflict to the nowadays very high success rates and low complication rates of CTO-PCIs being performed by experienced interventionalists. For instance, patients with prior CABG and a complex morphology of occluded native coronary arteries as well as consecutively occluded bypasses years after CABG surgery may benefit most from a technically demanding and long-lasting antegrade-retrograde but finally successful recanalization of native coronary arteries, as these patients may become free from limiting symptoms in daily life [22].

4. Antegrade recanalization techniques

The close cooperation of members of national and international CTO-expert groups such as the EuroCTO-club in collaboration with Japanese CTO-specialists refined and improved specific CTO techniques for more than 10 years. As a result, their experiences consolidated and were summarized including numerous publications about technical approaches and interventional steps in the so-called expert consensus statements [9, 23, 24].

The primary aim is to advance a coronary guide wire through the CTO lesion into the distal true lumen of the coronary artery. Most interventionalists at first apply a soft, polymer-jacked recanalization wire with a reduced tip diameter, which passes the CTO lesion in about 40% into the right direction usually through microchannels or soft tissue at the site of the occlusion. In the case of hard and severely calcified parts of the occlusion, a so-called "wire escalation strategy" is required using recanalization wires with increasing tip loads. Within a next step, a medium-heavy, very well guidable recanalization wire is used, when the course of the CTO lesion is unclear. In contrast, when the course of the CTO-lesion is recognizable again, a harder recanalization wire with a reduce tip diameter is used, which in turn reveals an increasing force to penetrate the CTO-tissue and is targeted actively into the true distal coronary arterial lumen. The correct distal position of the wire has to be confirmed in two different angulations by contralateral contrast injections through the contralateral coronary artery (i.e., from LCA in the case of RCA-CTO and from RCA in the case of LCA-CTO). This makes a double arterial access necessary for most CTO-PCIs. When the recanalization wire does not pass the distal end of the CTO into the true vessel lumen, the so-called "parallel-wire technique" may be applied. Here, the first wire marks the false pathway, whereas a second mostly harder wire is used additionally and usually enters then the distal lumen. A crucial technical device are microcatheters—catheters of very narrow diameters—which will be advanced over and to the tip of the recanalization wires. They secure the achieved recanalization pathway and thereby exchanging to other recanalization wires becomes possible.

After successful wire passage through the CTO-lesion, predilation with increasing balloon sizes will be performed with final implantation of drug-eluting coronary stents, which ensure valuable long-term results [25].

The success rates of the above-described antegrade recanalization techniques reach 55–80% depending of characteristics of patients and CTO lesions [26–29].

5. Retrograde recanalization techniques

In about 50% of CTOs, very complex occlusions are present being characterized by a straight nontapered proximal cap, long length or torturous course of the lesion, diffuse alterations of the distal vessel, or prior failures of recanalization attempts [20]. Retrograde recanalization techniques were introduced by Japanese CTO experts and have increased significantly the success rates of these complex CTOs without increasing peri-interventional complication rates [30–32]. The main goal of all retrograde techniques is to advance successfully a coronary wire to the distal end of the CTO lesion using collateral connections originating from the contra-lateral coronary artery. Additionally, ipsilateral retrograde techniques without using contra-lateral collaterals can be applied [33, 34]. **Figure 3** shows schematically an occlusion of the right coronary artery (RCA) and wire positioning using epi-myocardial collateral connections to the distal end of the CTO (**Figure 3A**, **B**). This retrograde wire marks exactly the distal end of the occlusion and can afterwards be targeted precisely by an antegrade wire, which will be able to be advanced antegradely and parallel to the retrograde "marker" wire into the distal vessel lumen (so-called "marker wire" technique, **Figure 3C**, **D**).

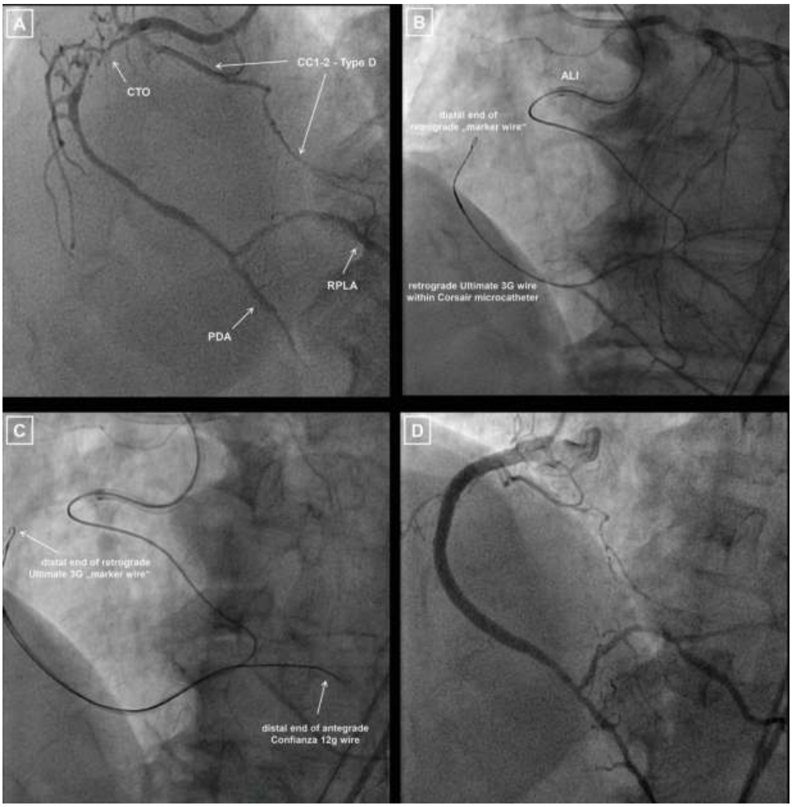

Figure 3. "Marker-wire" technique (CTO, chronic total occlusion) [34].

Occasionally, more complex retrograde techniques may be performed, such as the "reverse-CART" ("controlled antegrade and retrograde tracking")-technique [35, 36]. Here, balloon inflation over the antegrade wire creates space within the CTO lesion, which alleviates the entry of the retrograde wire, which may then advance parallel to the antegrade wire into the antegrade guiding catheter (**Figure 4A**, **B**). A consecutively introduced microcatheter protects

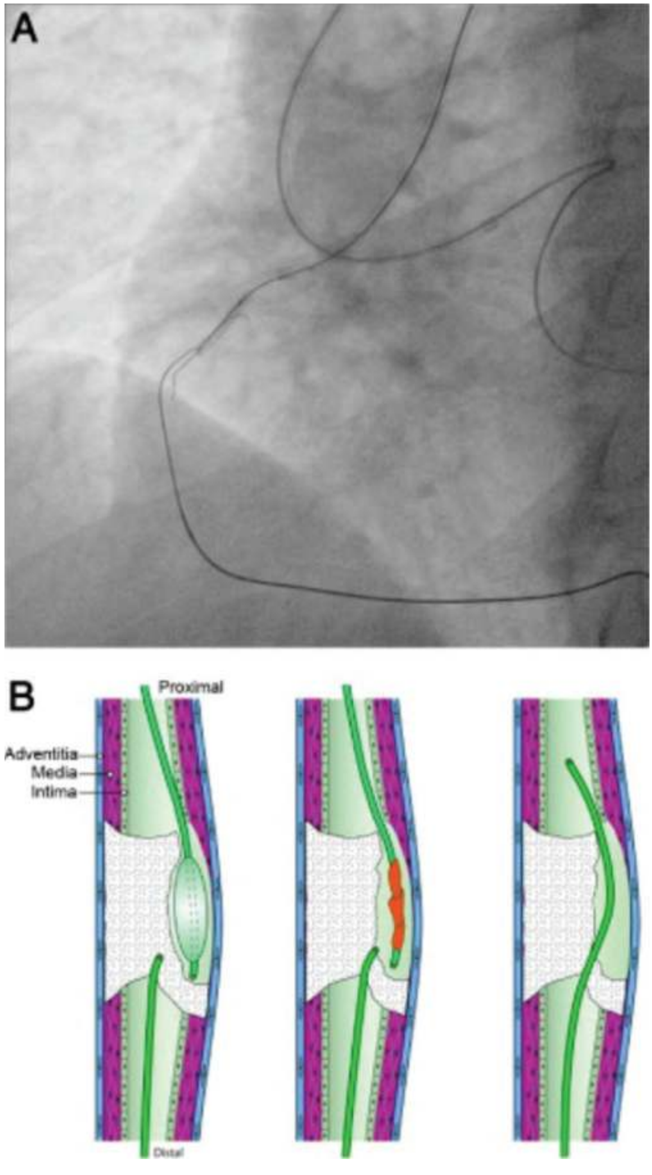

Figure 4. "Reverse-CART" ("controlled antegrade and retrograde tracking") technique [36].

coronary circulation, and within the microcatheter, a 330-cm long special externalization wire can be advanced from retrogradely and outside of the body (so-called "externalization"). After wire externalization, balloon dilation and stent implantation will then be performed antegradely using the externalization wire.

6. Recanalization strategies

Most CTO lesions can be recanalized by antegrade techniques. In about 30%, a retrograde technique is necessary due to the complex morphology of the CTO (**Figure 5**). An escalation of the recanalization strategy is valuable, because an antegrade attempt may be successful in the case of a complex morphology of the CTO. Retrograde methods reveal a high technical expertise and should only be performed independently by interventional cardiologists with sufficient training in antegrade techniques (i.e., >300 antegrade CTO-interventions, >50/year) and additional training in retrograde techniques (25 retrograde cases as second and primary operator each), as stated in a consensus document of the EuroCTO-club [9]. In the presence of high expertise in all recanalization techniques, availability of necessary specific materials and a possible widened indication up to 90% of CTOs can be recanalized. However, the high

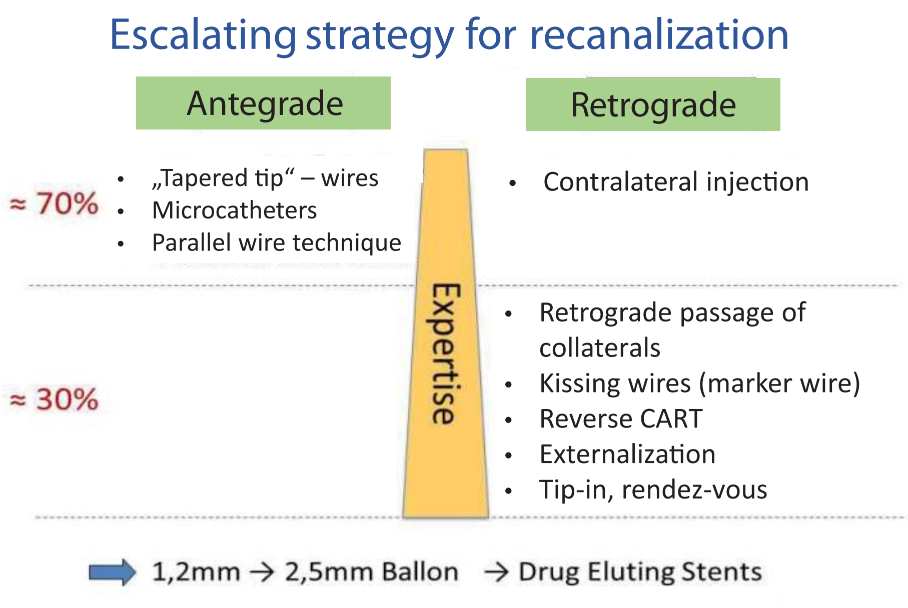

Figure 5. Escalating strategies for recanalization (CART, controlled antegrade and retrograde tracking).

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technical demand and effort in time with longer radiation exposure are justified only in recognition of a presumed clinical benefit for the individual patient.

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