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Current Cardiology Reviews, **2015,** ***11,*** **299-304**

The Hybrid Approach to Intervention of Chronic Total Occlusions

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Abstract: The "hybrid" approach to chronic total occlusion (CTO) percutaneous coronary intervention (PCI) was developed to provide guidance on optimal crossing strategy selection. Dual angiography remains the cornerstone of clinical decision making in CTO PCI. Four angiographic parameters are assessed: (a) morphology of the proximal cap (clear-cut or ambiguous); (b) occlusion length; (c) distal vessel size and presence of bifurcations beyond the distal cap; and (d) location and suitability of a retrograde conduit (collateral channels or bypass grafts) for retrograde access. Antegrade wire escalation is favored for short (<20 mm) occlusions, usually escalating rapidly from a soft tapered-tip polymer-jacketed guidewire to a stiff polymer-jacketed or tapered-tip guidewire. Antegrade dissection/re-entry is favored in long (≥20 mm long) occlusions, trying to minimize the dissection length by re-entering into the distal true lumen immediately after the occlusion. Primary retrograde approach is preferred for lesions with an ambiguous proximal cap, poor distal target, good interventional collaterals, and heavy calcification, as well as chronic kidney disease. The "hybrid" approach advocates early change between strategies to enable CTO crossing in the most efficacious, efficient, and safe way. Several early studies are demonstrating high success and low complication rates with use of the "hybrid" approach, supporting its expanding use in CTO PCI.

Keywords: Chronic total occlusion, percutaneous coronary intervention, retrograde.

INTRODUCTION

Percutaneous coronary intervention (PCI) of chronic total occlusions (CTOs) is challenging and technically demanding, but also rapidly evolving field, which has benefited from remarkable equipment and technique developments during the past decade [1-3]. These developments have led to significant improvement in both procedural success and complication rates [4, 5], as well as increased efficiency [6].

The main reason for CTO PCI failure is inability to cross the occlusion with a guidewire. There are three main CTO wiring techniques: antegrade wire escalation, antegrade dissection/re-entry, and retrograde; each with its own merits and limitations. The "hybrid" approach to CTO PCI (Fig. **1**) is an algorithmic approach to CTO crossing that focuses on opening the occluded vessel using all available techniques (antegrade, retrograde, true-to-true or intra-plaque lumen crossing or re-entry) tailored to the specific case in the most safe, effective, and efficient way [7]. The "hybrid" approach was created by consensus of several high-volume CTO operators who convened at a workshop in Bellingham, Washington in January 2011, and has been associated with high procedural success rates across several patient cohorts.

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DESCRIPTION OF THE "HYBRID" ALGORITHM

Step 1: Dual Injection

Dual injection is probably the most important step for increasing procedural success and decreasing complications in CTO PCI [8], and should be done in all patients with contralateral collaterals. Dual injection facilitates procedural planning by clarifying the location of the proximal and distal cap and the CTO length, which is almost always overestimated with single injections. It also allows evaluation of the collateral circulation to determine whether the retrograde approach is feasible. Additionally, dual injection can clarify the guidewire and equipment location during CTO PCI crossing attempts, making the procedure safer.

Dual injection is performed by first injecting the donor vessel, followed by injection of the CTO target vessel 2-3 seconds later. Low magnification can facilitate visualization of the entire coronary circulation, avoiding the need for panning. If automatic injectors are used, we recommend the use of the automatic injector on the retrograde side, and a regular syringe on the antegrade side, in order to avoid inadvertent antegrade injection during the procedure.

Step 2: Assessment of CTO characteristics

Detailed angiographic review is essential for CTO PCI procedural planning, and should ideally be performed by the

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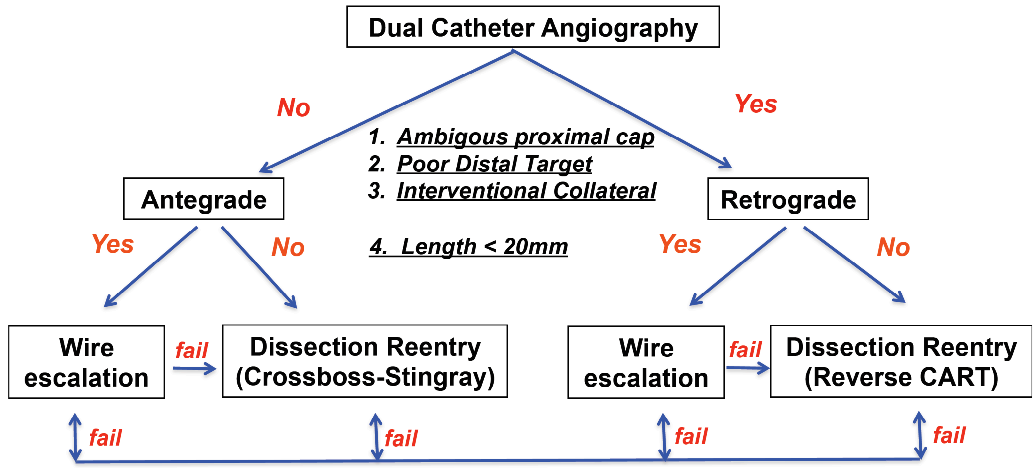

Fig. (1). Overview of the "hybrid" CTO crossing algorithm. The algorithm starts with dual coronary injection to allow assessment of several angiographic parameters, and allow selection of a primary antegrade or primary retrograde strategy. Strategy changes are made, depending on the progress of the case. Modified with permission from (7).

entire CTO PCI team. Often, 20-30 minutes of review is necessary to fully appreciate the CTO anatomy and determine the optimal action plan based on the "hybrid" algorithm. Ad hoc CTO PCI is discouraged because it cannot allow enough time for in-depth angiographic review. Moreover, staging the procedure will reduce radiation and contrast administration.

Dual injection focuses on assessment of the following four angiographic parameters: (a) morphology of the proximal cap (clear-cut or ambiguous); (b) occlusion length; (c) distal vessel size and presence of bifurcations beyond the distal cap (i.e., "landing zone"); and (d) location and suitability of collateral channels or bypass grafts for retrograde access (Fig. **2**) [1, 7, 9, 10]:

a. **Proximal cap location and morphology (Fig. 2A).** Clear understanding of the CTO starting point is critical for both success and safety. A clearly defined and unambiguous proximal cap favors up-

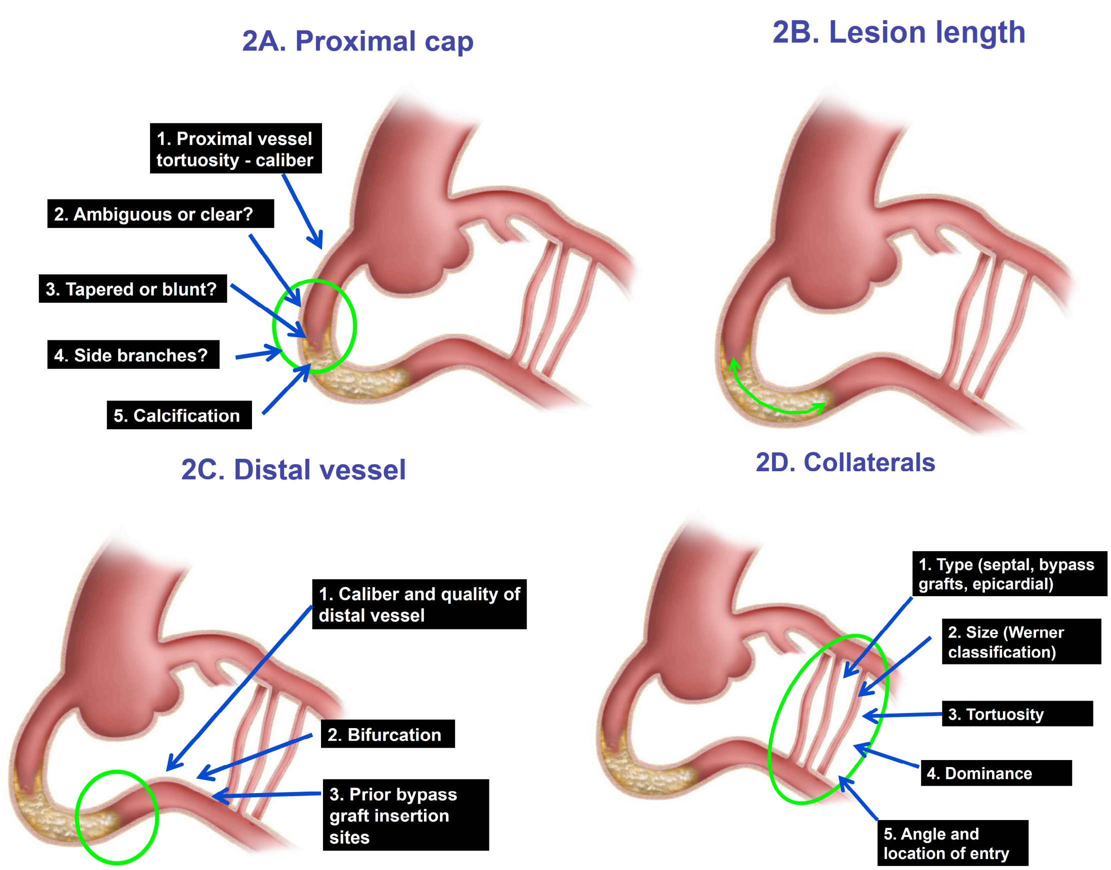

Fig. (2). Four areas of focus during assessment of the angiogram in patients with coronary chronic total occlusions.

front use of an antegrade approach, whereas a poorly defined proximal cap favors a primary retrograde approach. Unconventional angiographic projections may be needed to clarify the proximal location; for example, the lateral projection for right coronary artery occlusions. In some cases, angiography alone may be inconclusive, but intravascular ultrasound can help elucidate the proximal part of the CTO. Side branches at the proximal cap may hinder antegrade wiring, but could potentially be used for side branch anchoring to increase guide catheter support. Tapered proximal caps are more favorable than blunt caps and are part of the J-CTO (Multicenter CTO Registry in Japan) score for determining the difficulty of CTO crossing [11, 12].

b. **Lesion Length (Fig. 2B)**. The longer the lesion, the more challenging crossing is likely to be, especially when the occlusion is also tortuous and calcified [11]. Also, longer lesions are unlikely to be crossed with an exclusive intra-plaque course, the wire almost invariably entering and exiting the sub-intimal plane, even if a wire strategy is used. A useful cutoff point is 20 mm [11]: ≥20mm long lesion may be best approached with a primary dissection/re-entry strategy, whereas <20 mm long lesions are usually approached with antegrade wire escalation. Lesion length can be accurately assessed only by using dual injections. Alternatively, lesion length can be estimated by performing multiple detector computed tomography prior to the procedure.

c. **Target coronary vessel beyond the distal cap (Fig. 2C)**. The size and quality of the vessel distal to the occlusion significantly affects the difficulty and success rate of CTO PCI. Small, diffusely diseased vessels are associated with lower procedural success rates, in part due to difficulty re-enteringin the true lumen if subintimal guidewire tracking occurs. The presence of a bifurcation at the distal cap is also an unfavorable characteristic when dissection/re-entry strategies are being utilized because one of the branches may be compromised during re-entry attempts [13]. In patients with prior coronary artery bypass graft surgery (CABG) the distal vessel may be distorted at the distal anastomotic site, thus hindering wiring.

d. **Size and suitability of a retrograde conduit (Fig. 2D).** Several characteristics of the retrograde conduit are important, including type (septal, epicardial, or bypass graft), size, tortuosity, dominance (wiring the only collateral that supplies the vessel distal to the occlusion may cause severe ischemia), angle and location of entry into the distal vessel. Ideally, the collateral donor vessel would have minimal disease and tortuosity; otherwise, PCI of the donor vessel may be needed before retrograde CTO PCI. The collaterals should ideally enter the CTO vessel at a sufficient distance from the distal cap to allow enough "landing zone" for retrograde equipment. Septal channels can even be wired and crossed despite being barely visible, or even when they are invisible. Bypass grafts anastomosed to the target vessel can be also used as retrograde conduits to facilitate CTO PCI, even if they are occluded [14, 15]. The presence of well-developed and suitable collaterals favors earlier use of retrograde technique during CTO PCI, although this is highly dependent on operator experience.

Step 3: Antegrade Wiring

Antegrade wiring is favored as the initial approach in short (<20 mm long) occlusions, and is performed by using guidewires of increasing stiffness to cross a CTO. The initial choice of wires and subsequent escalation pattern is variable across operators and CTO PCI schools of thought, however, most operators currently start with a soft tapered-tip polymer-jacketed guidewire (such as the Fielder XT wire, Asahi Intecc; Nagoya, Japan). If this wire fails to cross, hybrid operators currently favor a rapid escalation using a stiff polymer-jacketed wire (such as the Pilot 200, Abbott Vascular; Santa Clara, California) if the course of the CTO is unclear, or a stiff tapered-tip guidewire (Confianza Pro 12, Asahi Intecc or Gaia 2nd, Asahi Intecc) if the course of the CTO is well understood. Shaping of the wire is crucial; a 1 mm short and about 30^{o} bend at the tip is typically used. Support from a microcatheter is also warranted.

Step 4: Antegrade Dissection and Re-Entry

The "hybrid" algorithm recommends upfront use of antegrade dissection/re-entry for long (≥20mm) lesions approached in the antegrade direction because of low likelihood of maintaining intimal wire position with antegrade wire escalation. Extensive dissection/re-entry strategies, such as the subintimal tracking and re-entry (STAR) technique, should be avoided because they are associated with high restenosis and re-occlusion rates [16, 17]. Limited dissection/re-entry strategies are preferred, as they limit side branch loss, stent length, and likely, the risk for restenosis [18].

Dissection can be performed either by advancing a "knuckle" created by bending the tip of a polymer-jacketed guidewire (usually Fielder XT or Pilot 200) or by using the CrossBoss catheter (Boston Scientific; Natick, Massachusetts) [19]. The CrossBoss catheter has a 1 mm round distal atraumatic blunt tip and is advanced using a rapid-spin technique [20]. The advantage of dissection compared to wire escalation techniques is the lower risk for perforation (the knuckle or the tip of the CrossBoss catheter are deflected by the adventitia and are unlikely to exit the vessel structure, whereas the tip of a guidewire is much more likely to perforate) and faster speed.

Re-entry can be achieved using guidewires or using the Stingray system (Boston Scientific). Wire-based re-entry can be performed with the "mini-STAR" [21] or the Limited Antegrade Subintimal Tracking (LAST) [22] techniques. The Stingray system consists of the Stingray balloon and guidewire. The Stingray balloon has a flat shape with two side exit ports, and is designed to self-orient one exit port towards the true lumen upon low-pressure (2-4 atm) inflation

[19]. The Stingray guidewire is a 12 gram guidewire with a 20 cm distal radiopaque segment and a 0.009" tapered tip with a 0.0035" distal prong, and is advanced through the side port of the Stingray balloon facing the distal true lumen under fluoroscopic guidance to achieve re-entry [20, 23-25].

Step 5: Retrograde

In the retrograde approach, the CTO is approached from the distal vessel by advancing a guidewire into the artery distal to the occlusion through a collateral vessel or bypass graft [26, 27]. The retrograde approach has been one of the major reasons for increased CTO PCI procedural success rates [28-31], but also requires specialized training and equipment. The retrograde technique is preferred for lesions with an ambiguous proximal cap, poor distal target, good interventional collaterals, and heavy calcification, as well as patients with chronic kidney disease (contrast use is limited by utilizing the retrograde approach) [1].

Step 6: Change

In addition to providing guidelines on selection of the initial crossing strategy, the "hybrid" approach advocates early *change* of crossing strategy if the initially selected approach fails to make progress within a reasonable period of time. This is a simple, yet radical conceptual change in CTO PCI. Prior to the "hybrid" approach, if an antegrade CTO PCI attempt failed, most operators stopped and re-attempted CTO PCI using an alternative strategy (such as the retrograde approach) during a repeat procedure. In contrast, in the "hybrid" approach change from one crossing strategy to another is often performed during the same procedure. Rapid change maximizes the efficiency of the procedure by minimizing the time spent on non-productive efforts. It also reduces radiation exposure and contrast utilization, which in turn increases the likelihood of procedural success. To allow for seamless and prompt changes, expertise in all crossing techniques (antegrade wire escalation, antegrade dissection/re-entry, and retrograde) is needed.

OUTCOMES WITH USE OF THE "HYBRID" APPROACH

Several studies were recently published demonstrating a positive impact of the "hybrid" approach in achieving high success and low complication rates (Table **1**) [10, 12, 32-36]. Moreover, the "hybrid" approach has been used as a framework for training interventionalists in CTO PCI.

Nombela-Franco *et al.* validated the J-CTO score in a series of 209 consecutive patients who underwent hybrid CTO PCI by a high-volume operator [12]. The J-CTO score was applied for each patient and discrimination and calibration were evaluated in the whole cohort, and according to the approach (antegrade 47% and retrograde 53%). Despite a mean J-CTO score of 2.18±1.26 (difficult cases), successful guidewire crossing within 30 minutes and final angiographic success were 44.5% and 90.4%, respectively. The J-CTO score demonstrated good discrimination and calibration [12]. However, the final success rate was not predicted by the J-CTO score. These findings suggest that a liberal use of a hybrid antegrade and retrograde approach and dissection-reentry technique is likely to overcome the impact of complexity on success rate [12].

Michael *et al*. described application of the "hybrid" approach in 73 consecutive CTO PCI cases performed by a single operator [10]. Dual injection was used in 78%. Tech-

Table 1. Publications on the use of "hybrid" approach to chronic total occlusion interventions as of May, 2014.

Author	Year	n	Comment
El Sabbagh [32]	2012	1	First published case report on use of the "hybrid" approach
Nombela-Franco [12]	2013	209	Technical success was 90.4%, despite mean J-CTO score of 2.18±1.26 (difficult cases). The J-CTO score demonstrated good discrimination and calibration. However, final success rate was not predicted by the J-CTO score with the hybrid approach.
Michael [10]	2014	73	Technical success was 90.4%. A crossing strategy change was needed in 44% of cases. Final successful crossing strategy was antegrade wire escalation in 50.0%, antegrade dissection/re-entry in 24.2%, and retrograde in 25.8%
Pershad [33]	2014	198	Technical success was 95.4% in the post "hybrid" algorithm group vs. 79.4% among patients treated before introduction of the "hybrid" algorithm.
Christopoulos [35]	2014	497	Technical and procedural success was achieved with the "hybrid" approach in 91.5% and 90.7% of cases, respectively, and were significantly higher than the pooled technical and procedural success rates from previously published studies (76.5%, p<0.001 and 75.2%, p<0.001, respectively). Major procedural complications occurred in 1.8% of patients, an incidence similar to that of prior studies (pooled rate 2.0%, p=0.72)
Christopoulos [36]	2014	496	Technical and procedural success was lower among patients with previous CABG (88.1% vs. 93.4%, p = 0.044 and 87.5 vs. 92.5%, p = 0.07, respectively).
Christopoulos [34]	2014	521	Technical success in the in-stent restenosis and de novo group was 89.4% vs. 92.5% (p=0.43), respectively; procedural success was 86.0% vs. 90.3% (p=0.31), respectively; and the incidence of major adverse cardiac events was 3.5% vs. 2.2%, respectively (p=0.63).

nical success was 90.4% and the incidence of complications was 4.1%. The primary approach was antegrade in 87.5% of cases, of which 39.1% underwent retrograde attempt after failure of the antegrade approach. The initial crossing approach succeeded in 54.8%, however, an approach change was required in 44% of cases with a mean of 3.6±1.4 approach changes. Antegrade wire escalation, antegrade dissection/re-entry, and retrograde crossing were utilized in 97.2%, 46.6%, and 46.6% of cases, respectively. Among successful cases, the final CTO crossing technique was antegrade wire escalation in 50.0%, antegrade dissection/re-entry in 24.2%, and retrograde in 25.8% [10]; which highlights the importance of expertise in all CTO crossing techniques to achieve optimal outcomes.

Pershad *et al*. reviewed outcomes before and after adoption of the "hybrid" approach in two high-volume centers [33]. In 660 cases (462 performed before and 198 performed after "hybrid" approach implementation), both technical (95.4% vs. 79.4%, P<0.001) and procedural (88.3% vs. 77.9%, P<0.001) success significantly improved. Antegrade wire escalation was used in 39.3% of cases, with an overall success rate of 87.1%; antegrade dissection/re-entry was used in 28.7%, with an overall success of 94.7%; and the retrograde approach was used in 35.3% of cases, with an overall success rate of 78.8% [33].

Christopoulos *et al*. analyzed outcomes of 497 CTO PCI cases from an ongoing multicenter registry (Prospective Global Registry for the Studyof Chronic Total Occlusion Intervention – PROGRESS CTO, NCT02061436) [35]. Technical and procedural success was achieved in 91.5% and 90.7% of cases, respectively, and were significantly higher than the pooled technical and procedural success rates from previously published studies (76.5%, p<0.001 and 75.2%, p<0.001, respectively). Major procedural complications occurred in 1.8% of patients, an incidence similar to that of prior studies (pooled rate 2.0%, p=0.72) [35].

In two subsequent analyses from the same registry the outcomes of patients with prior CABG [36] and those with CTOs due to in-stent restenosis (ISR) [34] were explored.

Thirty-five percent of CTO PCI patients had prior CABG. Prior CABG patients were older, had more coronary artery disease risk factors, and had less favorable angiographic CTO characteristics [36]. The retrograde approach was more commonly used among prior CABG patients (in 39% vs. 24%, p <0.001). Technical and procedural success was slightly lower among patients with previous CABG (88.1% vs. 93.4%, p=0.044 and 87.5 vs. 92.5%, p = 0.07, respectively), whereas major procedural complications were similar in the two groups: 1.1% among patients with prior CABG vs. 2.1% of patients without prior CABG [36].

CTO due to ISR represented 10.9% of the overall CTO PCI cases and was associated with higher frequency of diabetes, less calcification, but longer occlusion length [34]. Technical success in the ISR and de novo group was 89.4% vs. 92.5% (p=0.43), respectively; procedural success was 86.0% vs. 90.3% (p=0.31), respectively; and the incidence of major adverse cardiac events was 3.5% vs. 2.2% (p=0.63), respectively [34].

CONCLUSION

The "hybrid" approach to CTO PCI has emerged as a valuable guide to CTO PCI. It builds on the value of dual coronary angiography, and emphasizes the importance of careful and detailed review of the angiographic images to develop a procedural plan. The plan is flexible, allowing several "what if" scenarios. The "hybrid" approach enables excellent procedural results in experienced centers and forms a central platform for procedural planning and execution, as well as for teaching and widespread dissemination of CTO PCI techniques.

CONFLICT OF INTEREST

Dr. Spratt: consultant for Boston Scientific.

Dr. Rinfret: consulting honoraria/speaker fees from Terumo, Abbott Vascular, and Boston Scientific; research grant from Abbott Vascular.

Dr. Banerjee: research grants from Gilead and the Medicines Company; consultant/speaker honoraria from Covidien and Medtronic; ownership in MDCARE Global (spouse); intellectual property in HygeiaTel.

Dr. Brilakis: consulting/speaker honoraria from Abbott Vascular, Asahi, Boston Scientific, Elsevier, Somahlution, St Jude Medical, and Terumo; research support from InfraRedx and Boston Scientific; spouse is employee of Medtronic.

Remaining Authors: none.

ACKNOWLEDGEMENT

Declared none.

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Received: July 23, 2014 Revised: March 10, 2015 Accepted: March 11, 2015