New Advances in Chronic Total Occlusions

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Abstract

Coronary chronic total occlusions (CTOs) still represent the greatest technical challenge that interventional cardiologists face. CTOs remain seriously undertreated with percutaneous techniques, far below their prevalence. One reason for the low uptake was the suboptimal CTO percutaneous coronary intervention (PCI) success rates over a long period of time. During the last years, dedicated groups of experts in Japan, Europe and United States fostered the development and standardisation of modern CTO recanalisation techniques, along with providing focused training and proctorship worldwide. As a result, dedicated operators achieved success rates far beyond 90 %, while coping with lesions of increasing complexity. A series of studies, mainly retrospective and observational in nature, explored the prognostic impact of CTO PCI, revealing that successful lesion recanalisation is related to improved patient outcome and anginal status; further evidence from randomised trials is on the way. The following review reports on the most recent advances in the field of CTO recanalisation, in an attempt to promote a more balanced approach in patients with chronically occluded coronary arteries and encourage more operators to cope with these inherently complex lesions.

Keywords

Coronary chronic total occlusion (CTO), retrograde approach, collateral circulation, prognostic benefit, J-CTO, subintimal space, true lumen re-entry

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Coronary chronic total occlusions (CTOs) are identified in up to one third of patients with coronary artery disease referred for non-urgent coronary angiography,^{1,2} with an incidence increasing with age.³ Conceptually, you may argue that the motivation to reopen a totally blocked artery is not as strong as for subocclusive lesions, that have the potential to progress and cause acute events. The evidence for coronary chronic occlusions goes into the opposite direction, suggesting that when viability and ischaemia are present reopening a coronary CTO yields a greater benefit than reopening subocclusive lesions. Data from mainly retrospective and observational series relate successful CTO recanalisation with improved survival, improvement in anginal status and left ventricular function, increased exercise tolerance and decreased need for coronary artery bypass grafting (CABG).^{4–8}

CTOs still represent the most complex lesion subset that interventional cardiologists face. Lesions with severe tortuosities, calcifications or large bifurcations present technical challenges, but the success rate in expert hands remains far above 95 %.⁹ With the exception of dedicated centres applying new strategies, the success rate of CTO PCI was over long period of time in the range of 60–70 %, ⁵ considerably lower than the success rate in non-occlusive coronary artery disease. Restenosis and reocclusion were also high before the introduction of Drug eluting stents (DES).¹⁰ The perception that CTOs are challenging lesions with a low success rate, limited scope for revascularisation and questionable

impact on patient outcome led to underutilisation of percutaneous recanalisation, with the majority of lesions left to medical therapy or referred for surgical revascularisation. No more than 10 % of all CTOs have been treated with percutaneous techniques over a long period of time.^{1,3,11–14} The following review reexamines the evidence leading to this conservative attitude and reports the advances in the treatment of CTOs, promoting a more balanced and proactive approach in patients suffering of this often highly disabling condition.

Definition

A chronic total occlusion is defined as a complete interruption of antegrade coronary flow (thrombolysis in myocardial infarction [TIMI-0] flow) of greater than three months standing.¹⁵ The long persistence of the occlusion implies the development of collateral circulation and this leads to opacification of the occluded distal vessel during injection in most cases. The pattern of distal filling – anterograde or with flow coming retrograde from the distal vessel – clarifies whether we are dealing with a real occlusion or a functional subocclusive lesion. Occasionally, non-intralesional bridging collaterals may give antegrade flow to the vessel beyond the occlusion. The careful examination of the occlusion in multiple views delineates the extraluminal course of these collaterals. Intraluminal channels are demonstrated pathologically in the majority of cases and may play a role in facilitating wire crossing^{16,17}; yet they mostly remain

below the resolution of angiography (100 μ m) and, by definition, have no continuity throughout the occluded segment or they violate the TIMI-0 criterion.¹⁸

The second criterion of CTO definition, occlusion duration, is more difficult to assess. Three levels of certainty are commonly used; occlusion duration angiographically confirmed, clinically confirmed and undetermined.¹⁵ A previous angiographic study confirming the presence of the CTO for more than three months is available in less than 30 % of cases, if you exclude high volume CTO centres receiving patients after previous attempts. A history of an acute coronary event or of a sudden change in symptoms can be used as a clinical surrogate in the absence of angiographic confirmation. A greater than three months duration is also assumed when there is a clear angiographic pattern compatible with total occlusion in the absence of recent symptom deterioration or with new symptoms clearly caused by an acute lesion in a different culprit artery.

Prevalence and Occlusion Characteristics

The frequency of CTOs depends on the type of patients studied with an incidence ranging between 10 and 30 % of all coronary angiograms.¹² More recent reports tend to show a lower incidence, possibly explained by the universal use of primary angioplasty and early revascularisation in acute coronary syndromes. Still, silent ischaemia or presence of atypical symptoms misinterpreted at the time of the acute event account for the consistent persistence of CTOs in 18.4 % of patients even in the most recent series.¹ You may expect that in patients with acute coronary syndromes CTOs are less frequent. In reality, even in patients with acute ST segment elevation myocardial infarction (STEMI), the incidence is 13 %.¹⁹ Interestingly, this subgroup of patients has a particularly poor immediate and long term prognosis. The presence of a CTO in a non-infarct-related artery was found to be a strong and independent predictor for both early mortality (within 30 days after STEMI) and late mortality (from 30 days to five years after STEMI).^{19,20} Inability to provide collaterals to the occluded vessel and, vice versa, acute impairment of preexisting collaterals from the acutely occluded vessel to the CTO jeopardising a large myocardial territory are possible explanations of this phenomenon, which also explains the prognostic benefit of recanalising CTOs. Far greater prevalence of CTOs, exceeding 50 % of cases,¹ are identified in the subgroup of patients restudied after coronary artery bypass graft (CABG) implantation. Since interventions in degenerated bypass grafts have frequent embolic complications and poor long term durability, the recanalisation of the CTO in the native vessel is an appealing but often technically challenging alternative.²¹

Lesion characteristics play an important role in the likelihood of a successful recanalisation. Morino et al. introduced a lesion-related difficulty grading tool, the J-CTO score, based on a large series of antegrade recanalisations in Japan.²² Length greater than 20 mm, presence of a greater than 45 degrees bend within the occlusion, presence of intralésional calcification, delineation of a stump at the proximal end are four angiographic parameters shown to influence the percentage and time requested for antegrade recanalisation. With the addition of a fifth non-angiographic parameter derived from the clinical history, a previous failed attempt, it is possible to calculate the J-CTO score attributing to each of these parameters one point. 'Easy' lesions with a score of 0–1 had a success rate of greater than 90 % (97.8 % and 92.3 % respectively) and required a short time for wire crossing in most cases. Success progressively falls with an increased score

with 'difficult' – J-CTO score equal or greater than 3 – lesions having a 73.3 % success rate and demanding a prolonged time for crossing.²² Technical progress and the introduction of the retrograde approach have certainly modified these percentages, probably cancelling the importance of some of these factors and shifting the field from lesion-related to collateral circulation-related predictive factors of failure. The presence and quality of the collaterals, their continuity and tortuosity, their location in the septum or in the epicardium, the angle of the collateral anastomosis with the CTO vessel become important factors if a retrograde strategy is considered.²³ Non-invasive imaging, in particular coronary multi-slice computed tomography (MSCT), can help delineate the characteristics of the CTO, by definition invisible because not opacified. With coronary MSCT the occluded segment can be better delineated, calcium more reliably detected and quantified, the tortuosity and vessel path followed, the true length of the lesion better defined.

Rationale and Indications to CTO Recanalisation

Relief of symptomatic ischaemia and angina and improvement of prognosis are the ultimate goals of CTO revascularisation. Borgia et al. documented that successful CTO PCI is related to improved angina-related quality of life (QoL).²⁴ A number of retrospective reports and prospective registries have demonstrated that successful CTO revascularisation leads to enhanced left ventricular function tests and exercise tolerance, decreased need for CABG and improved survival and decreased cardiac mortality or complications in case of future acute events.^{4,5,7,19,20,25–28} Multicentre randomised trials, such as the EuroCTO trial, have been launched to further elucidate the prognostic impact of CTO revascularisation.¹⁵ In anticipation of the study results, the indications to revascularisation of CTOs should not differ from the indications to revascularisation of subocclusive lesions and can be defined based on a potential improvement of prognosis. The dimension of the occluded artery and the presence of other critically narrowed arteries weigh heavily in the decision to revascularise a CTO. Evidence of ischaemia and viability in the territory supplied by the occluded vessel, accompanied in most cases by anginal symptoms or anginal equivalents, should be confirmed.¹⁵

Imaging techniques are most suitable to define viability and ischaemia. Magnetic resonance imaging (MRI) can provide objective evaluation of pharmacologically-induced wall motion changes, precisely assessing myocardial fibrosis, perfusion²⁹ and viability. Subendocardial extent of the late gadolinium enhancement smaller than 50 % of the wall thickness with MRI and reversible perfusion deficit greater than 10 % of the total myocardial mass with myocardial nuclear perfusion are currently used as gold standards for viability and prognostically relevant ischaemia. Patients with poorly controlled anginal symptoms with medical therapy may also have indications to revascularisation.³⁰ A prerequisite to meet this indication is the optimisation of the dose and type of drugs, starting from beta-blockers, and the demonstration of objective evidence of ischaemia. Secondary causes of angina, such as anaemia or hyperthyroidism must be appropriately corrected. In theory, indications to surgery or angioplasty are based on the same criteria and the decision between one or the other is purely technical. Surgical revascularisation may be favoured in the presence of left main coronary artery disease, complex triple vessel disease (especially in patients with insulin-dependent diabetes, severe left ventricular dysfunction or chronic renal insufficiency), occluded proximal left anterior descending artery and multiple CTOs with a relatively low anticipated success rate.³¹ In practice, surgical

Figure 1: Intravascular Ultrasound (IVUS)-guided Chronic Total Occlusion (CTO) Recanalisation

A: Stumpless proximal left anterior descending (LAD) occlusion at the takeoff of a sizeable first Diagonal branch (D1). B: Right coronary artery (RCA) providing retrograde flow to the occluded LAD via tortuous epicardial collaterals. C: Gaia Second wire (Asahi Intecc, Japan) supported by a Corsair microcatheter (Asahi Intecc, Japan) at the assumed proximal cap of the occlusion. IVUS catheter (Eagle Eye Platinum ST Catheter, Volcano, USA) in D1 identifying the proximal CTO cap; the wire is not visualised and retrieved. D: Following IVUS guided puncture of CTO proximal cap, an IVUS pullback from the D1 (vessel relatively parallel to the occluded proximal LAD) confirms the intra-CTO site of the wire from distal to proximal part (numbers 1 to 4) of the occlusion (arrows). E: Final angiographic result after a 2.5x38 mm and a 2.25x23 mm everolimus eluting stents implantation.

Figure 2: Anterograde Recanalisation Using the Parallel Wire Technique

A: Right coronary artery (RCA) chronic total occlusion (CTO); blunt proximal stump and bifurcation at the site of CTO. B: Contralateral contrast injection revealing CC2⁴¹ septal and epicardial collaterals from the left anterior descending (LAD) coronary artery. C: Bilateral contrast injection with the distal vessel opacified indicating a short and straight occluded segment. D: To prevent dislodgment of the guiding catheter while pushing wire and microcatheter through the occlusion, a 2.5x20 mm balloon is inflated in an atrial branch proximal to the occlusion (anchoring technique). The wire (Fielder XT, Asahi Intecc, Japan) made progress through the body of the occlusion but clearly appears to have deflected from the target. E: A Confianza Pro 12 wire (Asahi Intecc, Japan) supported by a Corsair microcatheter (Asahi Intecc, Japan) is advanced parallel to the Fielder XT wire left in place and steered towards the distal end of the occlusion. F: Successful chronic total occlusion (CTO) crossing; dissection at the site of the occlusion after predilatation. G: Final angiographic result after implantation of 3.5x38 mm and 3.0x38 mm everolimus eluting stents. There is no residual stenosis and (thrombolysis in myocardial infarction [TIMI]) flow is normal.

indications are rarely given if there is no involvement of the proximal left anterior descending coronary artery. The decisions should be taken in an open discussion among clinicians, interventionalists and cardiac surgeons. Data from large national registries (British Cardiovascular Interventional Society (BCIS), Swedish Coronary Angiography and Angioplasty Registry (SCAAR), American College of Cardiology (ACC) Dynamic registry) suggest underutilisation of PCI for CTO, limited to 5-6 % of all the revascularisation procedures and far below its prevalence.^{12,32} The preference given to surgery is probably not justified because recent trials show that more than 30 % of occlusions initially scheduled for bypass implantation were not grafted because of poor distal vessel quality and the occlusion rate of vein grafts, the most frequently used conduits for right and left circumflex coronary arteries, remains suboptimal and in some series in excess of 50 %.

Technique of CTO Recanalisation with Angioplasty

Complete coronary occlusions have been approached by pioneers such as Kaltenbach and Reifart in Frankfurt or Hartzler and Rutherford in Kansas City more than 30 years ago, when the materials were often

inadequate and the reocclusion rate prohibitive.^{33,34} The introduction of laser wires and of various devices that expected to improve success rates led to a revival in enthusiasm for CTO treatment in the early nineties. It also fostered the use of methods due to become standard, such as bilateral contrast injection for visualisation of the distal occluded vessel and assessment of the collateral circulation. However it was only in the last decade that the utilisation of percutaneous CTO recanalisation became more widespread thanks to the availability of dramatically improved wires and dedicated microcatheters, and the introduction of DES drastically reducing late failure.¹⁵ Much effort has been put forth to develop techniques to tackle these complex lesions and provide operators with strategies to optimise their success rate. The increase of success rate from 50–60 % to 80–90% of all CTOs attempted does not tell the full story because many CTO lesions routinely attempted in the last years were not even considered before, except by very few highly committed operators.³⁵ Opening complex CTOs still remains a challenge requiring a certain learning curve before the operator becomes familiar and can be highly effective, while simultaneously keeping the procedure safe. An active CTO programme with specific proctorship and guided training are indispensable elements for a centre to obtain

Figure 3: Retrograde Recanalisation with a Reverse Controlled Antegrade Retrograde Subintimal Tracking (CART) Technique

A: Proximal right coronary artery (RCA) chronic total occlusion (CTO) with tapered stump. B: Contralateral injection revealing retrograde filling of the distal vessel via septal collaterals. C: Selective contrast injection through a Corsair microcatheter (Asahi Intecc, Japan) better delineates the course of the septal collaterals. D: A mid continuous septal collateral (Werner CC1 [41]) is selected and crossed with a Sion wire (Asahi Intecc, Japan). E: Corsair microcatheter advanced into the distal true lumen over the Sion wire; selective contrast tip injection confirms intraluminal position. F: Bilateral contrast injection through the antegrade guiding catheter (GC) and the Corsair delineating the occlusion's length. G: Antegrade wiring of the occlusion with a Gaia second wire. H: Bilateral wiring of the occlusion with a Gaia second wire antegrade and an Ultimate wire (Asahi Intecc, Japan) retrograde, both supported by Corsair microcatheters. I: Antegrade balloon dilations enlarging the subintimal space to facilitate retrograde wire crossing (reverse CART technique). J: Guideliner™ (Vascular Solutions, Inc., Minneapolis, Minnesota) facilitated retrograde wire (Ultimate) crossing; the Corsair is advanced over the wire through the Guideliner in the antegrade GC and the externalisation of an RG3 wire (Asahi Intecc, Japan) allows antegrade insertion of balloons and stents. K: Final angiographic result after implantation of 4.0 x18 mm, 3.5x33 mm and 3.0x33 mm everolimus eluting stents.

the success rates reported above and a minimal number of 50 CTOs per year is considered essential for an operator to maintain competence.^{15,36} In that direction, crucial was the rapid development of dedicated CTO PCI equipment, such as long sheaths to optimise back-up support, over-the-wire microcatheters for wire support and frequent reshaping and exchange, wires of escalating stiffness with high steerability and tapering. Balloon anchoring for active support and trapping of wires within guiding catheters to facilitate removal of long microcatheters are useful adjunctive techniques common to contemporary CTO PCI.¹⁵ Stumpless occlusions may benefit from identification of the proximal end of the occlusion with MSCT before the procedure and intravascular ultrasound during the procedure (see Figure 1). At present, CTO recanalisation strategy depends on two important parameters – coronary anatomy and operator experience both with antegrade and retrograde techniques. For operators experienced in all CTO techniques, anatomy dictates the strategy. Antegrade approach is successful in most cases and should be attempted first in the majority of the occlusions. Although a retrograde approach is needed only in a minority of lesions and collateral crossing can be very time consuming and unpredictable even in the best hands, greater than 80–90 % success rates are unattainable without the addition of 15–20 % retrograde success in lesions failed anterogradely or with no antegrade options (true ostial occlusions, unidentified stump, ambiguous track).³⁷

In case the antegrade wire cannot be advanced through the occlusion and appears to deflect to a subintimal position, a second wire can be directed towards the distal true lumen using the first as a marker (parallel wire technique) (see Figure 2). If the wire remains in the subintimal space for a longer track distal wire reentry can be attempted guided by ultrasound or using a dedicated flat balloon with lateral ports for wire exit (Sting-Ray™, Boston Scientific, USA).³⁸ Katoh established the modern era of retrograde CTO recanalisation, guiding the development of dedicated microcatheters (Corsair®, Asahi Intecc, Japan) and delicate highly steerable wires (Sion, Fielder XT-R, Asahi Intecc, Japan) for use of tortuous septal and epicardial collaterals to probe the occlusion retrogradely, joining antegrade and retrograde wires with balloon inflation in the occlusion.⁹ The externalisation of a long 330 cm 0.010 inch (0.26 mm) diameter RG3 wire (Asahi Intecc, Japan) after retrograde crossing post reverse controlled antegrade retrograde subintimal tracking (CART) became the final step in most of these complex procedures, providing excellent back-up support

and allowing antegrade completion of the procedure (see Figure 3). Second generation DES have been shown to reduce restenosis and reocclusion, while experienced operators have high thresholds for treating proximal or distal disease outside the occluded segment, often due to become less prominent and not flow limiting with the growth of the vessel after flow restoration. Recently Brilakis et al. codified a strategy of initial selection and rapid switching from antegrade to retrograde approach should the initial strategy fail based on lesion characteristics and response, developing an unconventional use of rapid wire progression in the subintimal space knuckling it against the occlusion.³⁹ The incidence of complications remains low when these procedures are performed by experienced operators and high volume laboratories, despite the long procedural duration and use of multiple aggressive wires and catheters.⁴⁰ Wire exits are the norm in these procedures and are uneventful if promptly recognised and addressed. Drainage of pericardial tamponade and sealing of perforations with covered stents or microcoils are very rarely required but can be life-saving and the operator should be familiar with their use.

Conclusion

Thanks to increasing operator experience and development of more sophisticated techniques, CTO PCI is currently achieving high technical and procedural success rates and serves as an efficient alternative to the established approach of these complex lesions (medical therapy or surgery). The high incidence of CTO requires good clinical judgment in the selection of the lesions in need of recanalisation. Recent guidelines have corrected the mistakes from the misinterpretation of trials exploring the clinical benefit of universal recanalisation of recent occlusions after STEMI (Occluded Artery Trial(OAT) trial), responsible for inappropriate restrictions in the use of PCI for these lesions.³⁰ Further technical development is needed to facilitate and simplify the revascularisation techniques, making them both safer and more standardised and predictable. Operator's ability and centre's experience play a key role in achieving final success, still highly variable from less than 70 % when bilateral injection, modern dedicated wires and retrograde recanalisation are not used to 80–90 % in an increasing number of high volume dedicated centres. Further evidence, ideally from randomised studies, of clinical benefit of these inherently complex procedures may encourage operators and centres to engage in this challenging endeavour. ■

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