BRIEF CLINICAL REVIEW

Chronic Total Coronary Occlusion

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Introduction

Chronic total coronary occlusions (CTOs) have been reported in up to 30% of patients with suspected or known coronary artery disease (CAD) who underwent diagnostic coronary artery catheterization.[1,2] These are defined as an angiographically documented or clinically suspected occluded segment with Thrombolysis In Myocardial Infarction (TIMI)-0 flow of greater than 3 months.[3] They occur most commonly in the RCA, with overall increased prevalence with increasing age.[4] In some cases, bridging collaterals may give the false impression of a functional sub-occlusive lesion due to antegrade flow to the vessel beyond the occlusion. Close examination of the occlusion from multiple views may allow outline of these collaterals outside of the vessel architecture. Coronary artery bypass graft surgery (CABG) has previously been considered the treatment of choice in CTO, more recent technical advancements and operator skill have led to higher rates of successful percutaneous revascularizations in CTO.

In the setting of acute myocardial infarction (AMI), the presence of a CTO in one or more of the non-infarct related arteries carries both a poor early prognosis and worse late outcomes even with successful primary percutaneous intervention (PCI).[5,6] The CTO vessel is unable to provide collaterals to the newly occluded vessel, and there may also be acute impairment of preexisting collaterals that had been supplying the CTO territory. Both of these situations increase the ischemic territory burden leading to worse outcomes with higher risk of cardiogenic shock, and higher mortality.[7,8]

Improved survival after successful CTO-PCI is attributed to several mechanisms. The recovery of myocardial contractile function in the CTO territory translates into a greater improvement of left ventricular (LV) function after a successful primary PCI; the prevention or reduction of left ventricular pathologic remodeling, and improved healing of the overlapping border in the infarct zone. Kirschbaum et al, investigated early and late effects of percutaneous revascularization for CTO on LV function and volumes. A positive effect on LV remodeling and ejection fraction was found both early (at 5 months) and late (up to 3 years). There was improvements in regional wall motion in the perfusion territory of the CTO which correlated with the extent of transmural infarction on pretreatment magnetic resonance imaging.[9] Other possible mechanisms include decrease of electrical instability and risk of fatal arrhythmias, and increased tolerance to further coronary ischemic events. Moreover, because CTO-PCI success is a prerequisite for achieving complete revascularization, a large majority of patients in the successful CTO-PCI group had complete coronary revascularization, which has been associated with improved survival in multivessel disease. A recent meta-analysis reports a 30% reduction in cardiac mortality in multivessel disease with complete revascularization compared to incomplete revascularization,[10] with CTO as the main determinant of incomplete revascularization.

CTO recanalization in cases with documented viability and ischemia in the territory distal to the CTO is supported by multiple studies. These studies have shown that successful CTO recanalization improves patient survival, improves anginal symptoms and left ventricular function, increases exercise tolerance, decreases need for Coronary Artery Bypass Grafting (CABG), and increases tolerance for future acute coronary syndromes.[11-13] Reports have also shown that a successful CTO-PCI may even reduce the risk for arrhythmic events in patients with ischemic cardiomyopathy.[14] The biggest challenge in CTO-PCI is success rate. Contrary to the high success rates in non-occlusive CAD, conventional CTO-PCI techniques were only successful in 60-70% of the cases.[15] Lesions with severe calcifications, tortuosities, or large bifurcations may be more technically challenging. Prior to the introduction of drug-eluting stents (DES), restenosis and re-occlusion rates were also high.[16,17] Only about 10% of CTOs have been treated with percutaneous techniques. The majority of patients have been treated medically or referred for CABG.[18] More recently, with advancements in the technology including specialized wires, microcatheters, balloons, and intravascular imaging, as well new techniques being applied by experienced operators, a 90% success rate has been reported.[19-21] The Global Chronic Total Occlusion Crossing Algorithm published in 2021 combines the experience of operators in 50 different countries and multiple crossing algorithms to present a standardized approach to advance the utilization and success rate of CTO-PCI.[20]

Randomized trials to elucidate the short- and long-term benefit of CTO revascularization are limited. The largest to date was the DECISION-CTO Trial with 834 patients randomly assigned to CTO-PCI vs medical therapy.[21] However, this study was designed as a non-inferiority study and limited by low power for clinical end points due to slow enrollment early trial termination. Also, almost 20% of patients in the medical arm receiving PCI crossed over. The EuroCTO trial enrolled a total of 396 patients to evaluate the safety of PCI, showed no

difference in cardiovascular death but an increase in ischemia-driven revascularization in the medical therapy arm at 3 years.[22] Further randomized trials are ongoing, including the NOBLE-CTO and ISCHEMIA-CTO trials to further evaluate the benefit of CTO on quality-of-life and major adverse cardiac events.[23]

The Pathobiology of CTO

Chronic total occlusion is characterized by a proximal fibrous, calcified cap which may be tapered. Generally, the body of the occlusion demonstrates neovascularization consisting of loose or dense fibrous tissue, atheroma, calcified tissue, and focal lymphocyte infiltrate.[24] In an autopsy series, Sakakura et al. showed negative occlusion remodeling is frequent in long-standing CTOs while shorter duration CTOs showed ample organized thrombus and large necrotic core. CTOs with CABG were extremely calcified. The distal cap of the occlusion tends to have a more tapered morphology than the proximal cap (78.9 vs 48.4 % in a recent series), which in turn facilitates distal wire entry with retrograde techniques.[25]

Interarterial collateral connections allow blood to flow to the vascular territory where the original blood supply has been compromised. These collaterals develop due to the shear forces exerted along the pressure gradient by engaging pre-existing interarterial connections.[26] Collaterals usually require 2–12 weeks to fully develop their functional capacity. CTO revascularization causes the regression of collaterals immediately following the re-establishment of antegrade flow and lasts for many months after the procedure.

Adjunctive Imaging

Adjunctive imaging has specific roles in CTOs. Noninvasive coronary imaging via Multislice computed tomography (CT) imaging has good sensitivity for calcium detection and even identifying late contrast filling of the distal vessel.[27] This allows for pre-procedural planning of both calcium burden and occlusion length, which are valuable markers of duration, complexity, and success of the recanalization procedure. The ability to also visualize the vessel in the occluded segment, especially if calcified, can also help the operator to understand where to pierce the proximal cap in stump less occlusions and to predict unusual courses, especially in very tortuous arteries. Viewing side-by-side CT images and angiography during the recanalization procedure is established practice in many active CTO laboratories. Algorithms for co-registration are designed to overcome the challenges of systo-diastolic and respiratory motion. Intravascular ultrasound (IVUS) is used in almost all cases by experienced Japanese CTO operators to better characterize the diseased segment after pre-dilatation, to ensure complete stent coverage, and to evaluate the stent post-deployment for appropriate expansion or complications, similar to the use of IVUS in other complex non-occlusive lesions. The specificity of IVUS during CTO recanalization allows identification of the vessel path in stump-less occlusions and the guidance of wire reentry especially during reverse Controlled Retrograde Anterograde Tracking (CART) technique. Optical coherence tomography (OCT) has limitations in the setting of CTO-PCI because of the need of forceful contrast flushing to clear blood. This is contraindicated in the presence of anterograde dissections, and with limited penetration of the near-infrared light.

Variability in the use of both non-invasive and invasive imaging during CTO recanalization is immense, ranging from more than 90% in Japan to less than 20% in Europe with intermediate penetration in the US. This may be partly due to availability and cost with all countries having progressive increased use, suggesting these methods are becoming an established tool for guidance of CTO recanalization. Therefore, IVUS-guided PCI could be more useful in CTO lesions by accurate assessment of stent size and treatment of suboptimal stent deployment such as under expansion, incomplete stent malposition, incomplete lesion coverage, or edge dissections.[28]

Conclusion

Randomized controlled trials have been limited to fully evaluate the long-term clinical outcomes of patients who have had CTO-PCI. They have shown that the procedure is safe compared to medical therapy. Registry and small non-randomized controlled trials show clinical benefit with improvement in ejection fraction, and symptomatic improvement. Due to historically low success rates and limited Coronary CTO-PCI. Over the past decade, CTO PCI success rates have increased due to advancement of technology, materials, education, training, and improved operator experience, along with the mastery of the antegrade approach and progression of the retrograde approach. This development is due to the dedicated groups of clinicians improving CTO-PCI. A standardized crossing algorithm may help improve success rates and broaden the patient population who may benefit from this procedure. Support of these sophisticated techniques from randomized controlled trials is necessary to increase future operator interest. CTO-PCI is a dynamic and evolutionary field, which will continue to flourish with the contributions and insight of experts. The current techniques provide a platform to engage current operators, encourage future adaptation and improved health care delivery worldwide.

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