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Review Article

Coronary chronic total occlusion intervention: A pathophysiological perspective

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ABSTRACT

Percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) is the last frontier in coronary intervention. PCI of CTO carries multiple advantages, such as significant improvement in symptoms, improvement in abnormal wall motion and left ventricular function and, possibly, increased long-term survival. As of today the procedural success is markedly improved because of technical innovations and is limited to highly experienced operators. To enhance the overall success rate from a worldwide perspective, a thorough understanding of its pathophysiology is critical to further development of newer techniques and technologies. In this review, the author outlines in-depth the evidence that underpins our understanding of CTO pathophysiology and its insight into CTO intervention that incorporates various steps and techniques to cross the lesion.

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1. Introduction

Percutaneous coronary intervention (PCI) of coronary chronic total occlusion (CTO) remains technically demanding and is considered as one of the last frontiers in coronary intervention. Referral for CTO PCI remains low in many countries despite the

Abbreviations: CTO, chronic total occlusion; PCI, percutaneous coronary intervention; MDCT, multiple detector computed tomography; IVUS, intravascular ultrasound; CART, controlled antegrade and retrograde subintimal tracking.

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reported success rates greater than 80% in Japan, USA and European centres.[1] Although plentiful retrospective data exist, there is lack of randomized trials supporting the benefit of CTO PCI on morbidity and mortality. This review aims to shed light on the development of techniques and strategies with an emphasis on procedurally relevant pathophysiology.

2. Pathophysiology overview

In essence, the majority of CTOs result from soft plaque rupture followed by thrombotic coronary occlusion and organization of thrombotic material. A minority of CTO results from progression of atheroma. Once coronary artery occlusion occurs, frequently the thrombus is propagated in a retrograde fashion from the point of occlusion to the proximal segment with a major side branch (SB).[2,3] This thrombus gets organized that is more rigid than fresh thrombus formation, with a dense concentration of collagen-rich fibrous tissue at the proximal and distal ends of the lesions, referred to as proximal and distal fibrous caps, respectively[3] with intervening occluded segments (Table 1). The occluded segment remains biologically active with recanalization, neovascularization, and inflammation giving rise to different composition of CTOs (Table 2).[2,4] The younger CTO lesions are observed to be predominantly soft or lipid laden whereas older lesions are typically hard or calcific.[2] Short duration CTO showed organized or organizing thrombus and presence of necrotic core. Srivasta et al.[2] documented age-related increase in the calcium and collagen content of CTOs which may be the substrate for inability to cross the occlusion with a guidewire. Increase numbers of intimal plaque capillaries are observed with increasing occlusion age. In CTOs less than one year old, the adventitia is the predominant vessel wall location of neovascular channel formation in terms of both number and size. In CTOs more than one year old, intimal plaque capillary numbers and size increase and are not significantly different from adventitia. The high frequency of large neovascular channels in all vessel wall locations even in CTOs of less than one year old duration reflects that the enlargement of growing neovascular channels within CTO is an early event.[2,5] The proximal cap often is fibrocalcific.[6] The distal cap considered to be less resistant than proximal cap, is conceptually important for development of retrograde techniques. This approach can be used after antegrade crossing failure or as an initial situations like ostial occlusions, long occlusions, heavy calcification, occlusions with ambiguous proximal cap, and occlusions with a diffusely diseased distal vessel, occlusion involving a distal major bifurcation and CTO vessels that are difficult to engage such as anomalous coronary arteries. The success of guidewire crossing in CTO PCI might be affected by loose fibrous tissue, pultaceous debris, or intimal plaque microchannels.[2]

CTOs exhibit two types of histological vascular channels that span the occluded segment.[2,5] Endothelialized microchannels (160–230 um) generated via neovascularization that connects the CTO from proximal to distal cap are termed histologically recanalized segments. Another type of vascular channels are micro capillaries (<100 um) that pass into the small SB or into the vasa vasorum, are termed non-recanalized segments as they do not span the CTO from proximal to distal caps. Short segment CTO with tapered tip stump (Fig. 1) is less likely to have a SB and more likely to have histologically recanalized segments than longer occlusions.[5] The tissue composition of tapered stump is characteristically looser fibrous tissue, with prominent neovascularization and recanalization. These recanalized segments (Fig. 2) may facilitate guidewire entry into distal true lumen within endothelialized microchannels. All occlusions with non-tapered or blunt stump have non-recanalized microcapillaries.[4] Srivatsa et al. demonstrated that older CTOs have greater calcification and fibrosis, fewer foam cells and macrophages as compared to younger ones.[2] Fuji et al. defined the proximal cap according to angiographic landmarks, and observed abrupt morphology change on intravascular ultrasound (IVUS).[6] Calcium was concentrated particularly in blunt stump proximal cap. A calcified arc was demonstrated in the wall opposite the SB. Suzuki et al. found moderately strong correlations between lesion age and indices of calcification demonstrated by IVUS. Very recent CTO with heavy calcium suggests that the CTO has arisen in a vessel with entrenched atheroma.[7] Guo et al. have suggested that the predominant virtual histology characteristic of CTO segments containing confluent necrotic core in contact with dilated guidewire track, is analogous to findings in non CTO vessels.[8]

The CTO has been traditionally divided into intimal and subintimal spaces which are key aspects of pathological information. The subintimal space lies external to the intimal layer but within the vessel architecture that includes the media (smooth muscle) and adventitia. During PCI, subintimal wire passage is within media between internal and external elastic membrane following the path of least resistance. Because of presence of histologically weak connective tissue, dissection in this area spreads easily and widely in both longitudinal and transverse direction. This subintimal space is considered to be the same space as the intramural hematoma in IVUS.[9]

Before formulating a strategy, the interventionist needs to perform a detailed review of the coronary angiography and scrutinize various regions of the artery carrying the CTO lesion

Table 2
Histological Components of Chronic Total Occlusion.[4]

Consistency	Components of occlusion
Very soft	Recanalized lumen, microchannels
Soft	Thrombus, proteoglycans, cholesterol clefts
Firm	Collagen, elastin
Hard	Calcium

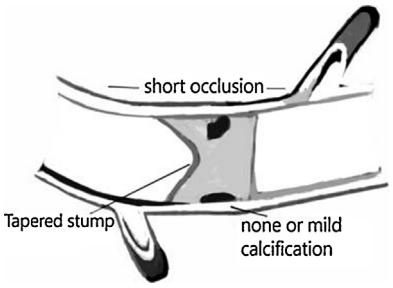

Fig. 1. Short segment CTO with tapered stump with mild or no calcification.

Table 1
Chronological Pathology of a Coronary Chronic Total Occlusion.

1. Acute phase: Obstructed lumen typically consists of ruptured plaque and thrombus.
2. Early phase: Deposition of proteoglycan matrix
3. Late phase: Negative remodeling consisting of dense collagen and calcium deposit
4. Late phase: Without negative remodeling, the presence of large micro-channels suitable for wire crossing

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