Applied Pathology for Interventions of Coronary Chronic Total Occlusion

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Abstract: Percutaneous coronary intervention of chronically occluded vessels can result in significant improvement in symptoms, relieve myocardial ischemia, and affect a reduction in major adverse cardiac events. Likelihood of achieving successful revascularization can be significantly enhanced with a thorough understanding of the pathology of these occluded coronary arteries. In this chapter, various steps and techniques to cross the CTO lesion and recanalize it are discussed in details.

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

INTRODUCTION

Chronic total occlusion (CTO) is defined as a coronary segment without antegrade flow (TIMI 0) and of duration greater than three months. An understanding of various pathology features in a CTO lesion would help the interventional cardiologist to successfully cross and recanalize it.

PATHOLOGY OVERVIEW

The majority of CTOs result from soft plaque rupture of an acute coronary syndrome (ACS) lesion, followed by thrombotic occlusion and organization of thrombotic material. A minority of CTO results from progression of atheroma. Once there is thrombotic occlusion, the thrombus will be propagated in a retrograde fashion from the point of occlusion to the proximal segment with a major side branch. The occluded segment remains biologically active with recanalization and inflammation [1]. The proximal edge of thrombus propagation is the site of the development of a proximal cap with fibrous and calcific atheroma [1]. As a result, the morphologic characteristics of a CTO lesion change according to its stage of formation or age (Table **1**).

STRATEGIC MAPPING

Before formulating a strategy for revascularization of a CTO lesion, the interventional cardiologist needs to perform a detailed review of the coronary angiography and scrutinize various regions of the artery carrying the CTO lesion (Table **2**).

In each segment of the CTO lesion, its complexity and severity depends on the pathological composition, the degree of calcification, the tortuosity, length or thickness of the segments and at the end, the presence and sizes of the

Table 1. Chronological pathology of a total coronary occlusion.

1.	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

Table 2. Areas of focus in a CTO lesion.

1.	Proximal segment
2.	Proximal cap
3.	Body of lesion
4.	Distal cap
5.	Distal segment
6.	Extraluminal pathology (subintimal tract, calcification)
7.	Antegrade and retrograde collaterals

micro-channels. However, the chance of success in crossing a CTO lesion depends on two important factors: the amount of significant fibrous and calcific material, and the presence and size of the micro-channels.

PATHOLOGY OF THE PROXIMAL SEGMENT

At the beginning of the session plotting the strategy for PCI of a CTO lesion, the coronary segment proximal to the

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CTO lesion is scrutinized for its length, tortuosity, calcification, and presence of collaterals and side branches (SB).

TECHNICAL APPLICATIONS

It is ideal to have a large 7 or 8-French extra back-up guide positioned co-axially in the ostium of the coronary artery. Coaxial engagement of the guide would ensure a smooth advancement of hardware into the target area.

If the proximal segment is too short, there is not enough landing zone for a large guide and it may be disengaged from the ostium. The heavy calcification of the proximal segment is another impediment to delivery of hardware to the proximal cap. This problem can potentially be overcome by using a buddy wire or the anchor technique in which a balloon is placed in the SB to immobilize the guide while advancing the hardware. If there is a SB at the proximal cap, then the wire may be preferentially deflected towards the SB rather than grinding through the true lumen of the CTO [2]. If there is a SB in the proximal segment, this SB could be used to position a small balloon inflated at low pressure to act as an anchor to the guide. If the CTO lesion is located in the distal segment of the coronary artery, then the tip of the guide can be extended using a GuideLiner (Vascular Solutions, Minneapolis, MN, USA). This is called the mother-and-child technique.

If there are antegrade bridging collaterals from the proximal segment, extra care should be exercised to avoid damage of these micro-channels. However, if there are retrograde collaterals, manipulation in the proximal segment across the length of the CTO would be relatively safer, as the distal segment is still perfused by the retrograde collaterals.

PATHOLOGY OF THE PROXIMAL CAP

The CTO lesion starts at the proximal cap. Usually, the cap is made with a dense concentration of collagen-rich fibrous tissue laced with calcium. The cap frequently contains micro-channels (200 μm in diameter), which are potential routes for wire crossing

TECHNICAL APPLICATIONS

If the proximal cap has the form of an angiographically tapered occlusion, the tapering stump is the starting place to probe the occlusion with a wire. In contrast, if the proximal cap has the form of a blunt (non-tapered) occlusion, it is necessary to look for the 'dimple sign' that is the hallmark for entry point [3]. However, if the stump is eccentrically oriented, there is a higher chance of subintimal wire passage. When there are extensive bridging collaterals (caput medusae), the chance of wire crossing decreases. The reason is that these intracoronary collaterals consist of dilated vasa vasorum, which are very fragile and easily perforated [3]. When there is a SB arising near the entry site of the CTO, the wire will often repeatedly deflect into the SB. However, due to high shear stress, a plaque is believed to build up on the opposite side of the origin of a SB and this may point to the path of the main vessel course [3].

In several cases when the guide disengages with a wire tip pinpointed to the center of the occlusion, either exchange the guide for a stronger backup or use a microcatheter. If the wire still cannot cross the proximal cap, intravascular ultrasound (IVUS) can be helpful to examine plaque composition, which could help guide the next strategy. When there is a SB coming out next to the proximal entry of a CTO lesion, an IVUS transducer can be placed in this proximal SB for interrogation of the CTO lesion in the main artery [3].

PATHOLOGY OF THE BODY OF CTO LESION

Once a wire crosses the cap at the dimple or through a micro-channel, the wire enters the body of the CTO lesion. At this point, factors which impact further progress include: (1) the type of tissue (loose versus dense fibrous tissue), (2) the amount of calcium deposits, and (3) the availability of large micro-channels.

PATHOLOGICAL COMPOSITION

A relatively recent CTO lesion is composed of proteoglycans which make up a major part of the extracellular matrix, the material between cells that provides structural support. Because proteoglycans are negatively charged, they attract positive ions, such as calcium. In a newly formed CTO, calcium deposits are sparse [4]. In contrast, in an older CTO, the occluded lumen is likely to have dense collagen, multiple calcium deposits, and fewer micro-channels. A plaque is considered soft if it has more than fifty percent of cholesterol and macrophages with loose fibrous tissue, while a hard plaque is more fibro-calcific with more than fifty percent collagen/calcium deposits filling the true lumen [4]. Continuous loose tissue is frequently seen in the tapered entry type of CTO as well as in the short-occlusive-length CTO; the loose tissue was located continuously from the proximal to the distal end [4]. In the middle of these loose or hard tissues, along the body of the CTO lesions, there are micro-channels.

These neovascularisation channels are approximately 200 microns in diameter, which is slightly smaller than the tip of a tapered wire. Their wall is made of a single cell layer so they are very fragile. In the remodeled type of CTO secondary to the shrinkage of the internal elastic lamina, the number of micro-channels is low. In the non-remodeled type, the CTO lesion has less fibrous tissue with numerous and larger micro-channels. These microchannels often extend to the small side branches and vaso vasorum, whereas others continue longitudinally from the proximal lumen to the distal lumen [4]. The longitudinal continuity of microchannels extends to approximately 85% of the entire CTO length, except in the early phase of CTO [4, 5].

TECHNICAL APPLICATIONS

Lesion Length

The length of the occluded segment is the most important factor which impacts the success of crossing a CTO. A length greater than 20 mm was a stronger predictor of failure to cross than calcification, tortuosity, blunt stump, or a previous unsuccessful attempt [6, 7].

Crossing the Length of the CTO by Tracking Loose Tissue

In the loose tissue tracking technique, the tip of an intermediate-strength wire is bent at 45–60° at the distal 1-2 mm, so the wire tip can be controlled and directed and it will not penetrate hard atherosclerotic plaque [3]. Wire handling tends to be similar to acute myocardial infarction cases, in that the wire is advanced easily and smoothly, with minimal rotations of the wire tip [3].

However, if the intermediate-strength wires cannot penetrate the space between the loose and dense fibrous tissues, at this point, an over-the-wire support system can be advanced and the wire is exchanged for a stiffer one with a tapered-tip end. This stiff and tapered-tip wire has a greater probability of penetrating the dense connective tissues into the distal true lumen than conventional wires [3]. When it is impossible to cross the wire with loose tissue tracking, the wire should then be manipulated into the intimal plaque, subintimal space, or in a retrograde fashion depending on the strategy of the operators [3].

Intra-luminal Tracking

Once the wire crosses the proximal cap, there is little tactile feel during lesion penetration. If the wire is in the true lumen, the wire would advance relatively smoothly [3]. The only way to know whether the wire is in the intima is to pull it back 1–2 mm. If the tip is in the intima, the operator would feel an unusual and unmistakable sensation of being stuck. A good rule of thumb would be that if any crunchy sensation is felt from the hard tissue at the wire tip, the operator can be certain that the tip is in the intima [3]. Inside the true lumen, the resistance of the intimal tissue surrounding the wire tip is relatively high but homogenous, so the wire tip trends toward the true lumen rather than the subintimal space. Yet even with intimal plaque tracking, the existence of high-resistance plaques such as fibrocalcific or dense calcium islands prevents the advancement of the wire across to the whole body of the CTO lesion resulting in procedural failure [3].

Lesion calcification or occluded stents serve as guideposts of the vessel course. When negotiating an angulated segment in the vessel, the wire should be steered toward the inner curve to avoid extraluminal passage [1]. If unsuccessful, then the next tactic is to venture into the subintimal track.

Subintimal Tracking

The subintimal space is constrained by fibrous and calcified tissue derived from atheroma on the luminal aspect and elastic adventitia on the external aspect of the vessel [8]. A free movement of wire tip during rotation and lesser resistance to advance is a mark of a subintimal position (the wire turns around the vessel lumen, giving the appearance of lengthening the tip curve [3]. The wire is considered completely in the false lumen when the resistance of the wire tip to advancement decreases [3].

The resistance of subintimal tissue against the wire tip is much lower than that toward the true lumen; therefore, the wire seems to easily remain in the subintimal layer, making it hard to redirect the wire tip toward the true lumen, resulting in failure to enter the distal true lumen, if only the wire techniques are used [3]. However, with the advent of re-entry devices such as a stingray balloon (Boston Scientific, Natick, Massachusetts), re-entry can be achieved into the distal true lumen, as long as the subintimal space is not too large.

Another limitation of subintimal tracking is reduction and loss of opacification of the distal vessel, which is likely to be due to a hematoma in the subintimal space compromising filling. Bleeding might be from disruption of neovascularization channels, or filling of the space with blood at systemic arterial pressure [6, 7].

Distal Cap

The distal cap is made of fibrous tissue and calcium; however, it is less resistant than the proximal cap.

Technical Applications

The presence of a tapering distal portion and chronic buildup of jagged hard plaque around the true lumen can make it extremely difficult for the wire to penetrate the distal cap [2]. Another important piece of information is where the collateral enters the arterial segment beyond the CTO. Is it at its distal or mid segment? The suspicion is, if there is any plaque or stenosis at the distal end, then the collaterals would enter the artery in the middle of the CTO segment [3].

Collateral Biology

Collateral vessels originate as arterioles connecting the vascular beds of visible coronary arteries. In the presence of CAD, significant pressure differences between coronary territories lead to dilatation of these collaterals and thus an increased blood flow [5]. However this process requires approximately 2 weeks to attain maturity and acute thrombotic occlusion in acute myocardial infarction often occurs more rapidly than the process of arteriogenesis required to develop a completely protective collateral circulation [9]. After PCI of the culprit artery, reduction in flow of the feeding collaterals is more rapid in the intramyocardial vessels than in the large caliber epicardial collaterals. These channels do not regress completely, but protection offered by these residual channels against subsequent events in the previously occluded vessels, most notably stent thrombosis, is quite limited [10].

TECHNICAL APPLICATIONS

Angiographic Search of Collaterals

Lower magnification and the avoidance of panning is of considerable help in evaluating collaterals (CC), because CC filling will invariably occur in a dissimilar time frame from the epicardial vessels. It is often the circumstance that a single frame or two in an entire series of angiograms will relay the appropriate information to determine the therapeutic strategy.

Utilization of Collaterals for Retrograde Wiring

Among the two potential channels for retrograde wiring, the septal collaterals are safer and should be the default

choice whenever possible [3]. Complications such as wire perforation in a septal collateral may not be a major problem and resolves spontaneously. However, a haematoma in a septal branch could cause hypotension due to obstruction of the left ventricular outflow tract. Considerable septal tortuosity is a major limitation to wire advancement, whereas size is less so. In general, the less tortuous septal collateral that connects should be considered as a first choice [11]. If an epicardial collateral is big enough to advance a balloon or microcatheter through it, this epicardial channel could be used.

When the epicardial channel is a major collateral source to the recipient artery, remote ischemia may occur and cause discontinuation of the PCI procedure [3]. During the wire manipulation in the channel, there is some risk of wire perforation which is a serious complication and can rapidly cause tamponade. An attempt can be made to control the perforation by inflating a balloon in the proximal segment [3]. Furthermore, balloon dilation of the epicardial channel should always be avoided as it may cause vessel rupture and cardiac tamponade. In patients who have already had coronary artery bypass graft (CABG), the chance for tamponade is lower because the pericardial space is already open [11].

CONCLUSION

Percutaneous coronary intervention of chronically occluded vessels can result in significant improvement in symptoms, relieve myocardial ischemia, and affect a reduction in major adverse cardiac events. Likelihood of achieving successful revascularization can be significantly enhanced with a thorough understanding of the pathology of these occluded coronary arteries, which can be applied at various steps of these challenging procedures.

DISCLOSURE

"A part of this article has already been published in Practical Handbook of Advanced Interventional Cardiology, Fourth Edition, 2013 DOI: 10.1002/9781118592380.ch10".

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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