Chronic total occlusions (CTOs) represent a fascinating and dynamic niche in the realm of coronary artery disease (CAD). Although the true prevalence is uncertain in the population at large, it has been estimated to be present in approximately one third of all patients with known or suspected CAD undergoing angiography. Approximately 10% of all attempted percutaneous coronary interventions (PCIs) are on CTOs, although the number varies considerably between operators, institutions, and countries. The choice of therapy has shifted to the use of stents in the majority of these cases. Because crossing a CTO lesion represents the major obstacle to therapy, interventional success has been linked to operator’s experience.

To improve success, novel devices and ingenious approaches have been developed to assist the operator in recanalizing lesions. We will discuss the use of such strategies, in particular, the use of intravascular ultrasound (IVUS) for treatment of CTOs.

**Development of CTOs**

The number of patients with persistent coronary occlusion declines over time likely due to spontaneous recanalization with approximately 30% of patients having a CTO 3 to 6 months after ST-elevation myocardial infarction (STEMI). With the introduction of primary angioplasty or stenting during evolving STEMI, the presence of a CTO at 6 to 7 months is reduced further to 5% to 12%. As CTO lesions age, morphologic changes occur within the plaque itself. A review of the histologic characteristics of CTOs offers insight into both the temporal evolution as well as the relative quagmire that awaits the interventional cardiologist.

CTOs often have neovascular channels that have grown through the occluded segment to provide distal flow, and these CTOs are considered “functional” occlusions. Independent of these small throughways, there is a progression of the composition of the plaque in the occlusion segment from cholesterol to foam cells in younger CTOs and to more fibrocalcification in older CTOs. IVUS can play an important role in differentiating the plaque components and facilitating differentiation between older and younger occlusions, which may have different outcomes and specific therapeutic strategies. The use of IVUS before angioplasty can easily assess the luminal geometry of both the proximal and distal vessel references, which is critical for strategy planning and device sizing. Previous IVUS studies have proposed the analysis of two proximal reference segments to estimate the age of the CTO: one measurement should be performed immediately proximal to the occlusion and another reference point would be away from the occlu-
Figure 1. Angiography demonstrating subintimal staining of the left anterior descending (LAD) artery after an unsuccessful attempt to cross a CTO (A). The wire was intentionally inserted into the subintimal space; a 1.5-mm balloon was passed for delivery of the IVUS catheter (B). The IVUS catheter in the false lumen (white arrows and circles indicate collapsed true lumen) (C). Failed cannulation of the true lumen with the Miraclebros 12 wire (Abbott Vascular, Redwood City, CA) (D). Successful cannulation of the true lumen with the Confranza wire (Abbott Vascular) (white arrow indicates IVUS confirmation of the Confranza wire) (E). The Confranza wire is advanced through the mid-LAD and into the septal perforator (F). IVUS confirmation of the wire in the LAD (G). IVUS of the LAD after balloon dilation (H). Final angiography after placement of three Cypher stents (Cordis Corporation, a Johnson & Johnson company, Warren, NJ) (I).
The rationale behind such a proposition is based on the potential shrinkage of the vessel triggered by the fibrotic development of a CTO. Such assessment can be helpful to define the age of the CTO because matured CTOs tend to have a smaller reference area due to fibrotic development. However, retrograde thrombosis from stagnant blood in the segment proximal to the culprit lesion and the presence of side branches represents a limitation of the IVUS approach.

SURVIVAL OUTCOMES FOR CTOs

The ultimate goals in treating CTOs are the relief of anginal symptoms, improvement in left ventricular ejection fraction (LVEF), and the freedom from subsequent CABG. Not surprisingly, the single most important predictor of attaining these goals is the success of the procedure. The short-term risk associated with CTOs is almost exclusively related to procedural complications. PCI of CTOs has been empirically associated with low risk, but there is an increase in short-term events in the overall population undergoing PCI of CTOs versus a matched non-CTO cohort. Yet, with procedural success, there was no difference in 10-year survival for PCI of CTOs versus matched non-CTOs. In selected centers with experienced operators, in-hospital major adverse cardiac event (MACE) rates as low as 6% have been reported. However, there has been minimal improvement in in-hospital MACE rates in less-experienced centers, despite improvements in techniques and equipment.

SUCCESS IN PCI

The rate of unsuccessful revascularization for CTOs has been reported as high as 30% to 40%. The mechanism of failure is largely attributable to inability to pass the guidewire and to a lesser extent, the inability to advance or inflate the balloon. Techniques to improve outcomes include the use of dedicated guidewires and multiple guidewires, as well as intracoronary fibrin-specific lytic infusions in patients with failed previous PCI for a CTO.

Although success rates have increased significantly, there is room for improvement. Use of adjunctive, intracoronary imaging to better visualize the true lumen and verify wire location potentially improves angiographic success, decreases rates of complications due to vessel dissection, and reduces fluoroscopic times.

IVUS

IVUS has been widely used to survey the extent of luminal stenosis, estimate the length of the diseased coronary segment, and analyze the histologic makeup of coronary lesions. IVUS also enhances the ability to identify the coronary anatomy, especially the location of branch points, and allows visualization of the true lumen in diseased segments. IVUS is a well-suited tool for the treatment of CTOs.

Use of IVUS for Balloon and Stent Size Selection

Routine use of IVUS for proper stent sizing and verification of adequate stent apposition has been suggested. Although the average cost of this technique is higher than conventional angiographic-driven stent delivery, it may be offset by reducing acute vessel closure. Due to diffuse atherosclerosis of the reference “normal” vessel, it has been shown that using angiographic data alone leads to underestimation of balloon and stent sizing. Use of IVUS before an intervention has been shown to lead to an increase in average balloon and stent size, with an increase in resultant luminal area by approximately 45% as compared to conventional angiography alone. The importance of proper sizing and apposition of intracoronary stents cannot be understated. Incomplete stent apposition has been shown to be prevalent in a large proportion of patients presenting with late stent thrombosis after DES implantation.

Use of IVUS for PCI of CTOs

It is important to note that the main use of IVUS for PCI of CTOs is primarily for balloon and stent sizing. However, various methods have been described for the technical use of IVUS in treating CTOs. We describe three examples: the false lumen method, the branch vessel method, and IVUS for salvage PCI.
False Lumen Method

The false lumen IVUS technique is reserved for those cases in which distal lumen access cannot be achieved using conventional wire techniques. The wire is maintained in the subintimal space, and a 1.5-mm balloon is used to dilate the vessel and create a tract to allow access to the IVUS catheter. IVUS images can show the true lumen, which is usually collapsed due to lack of blood flow. A second wire is inserted while the IVUS probe is maintained in the subintimal space to either guide the wire insertion or confirm its presence in the true lumen. Figure 1 illustrates this technique and shows an occluded LAD artery that could not be recanalized using the conventional wire technique. After multiple attempts, an IVUS catheter was introduced to guide the wire. After failure with the Asahi Miraclebros 12 wire, a second wire (Asahi Confianza) was able to cannulate the collapsed lumen visualized by IVUS imaging. After confirmation by IVUS and angiography, a microcatheter was used to exchange the Asahi Confianza for a Miraclebros 3 wire. The LAD artery was predilated, and three kissing Cypher stents were placed without difficulty.

IVUS as Salvage

IVUS use in a bailout situation in which stents have been inadvertently placed in the subintimal space has been reported. Although stent deployment should never occur without visualization of the distal vessel and confirmation of good distal runoff, this technique could be of assistance in such a scenario. Identifying the location of the true collapsed lumen can be accomplished with the assistance of IVUS. The reported case describes this technique. Repeat stent placement accomplished restoration of flow to the true lumen and distal vessel.

Implications of IVUS on Procedural Time

Procedural and fluoroscopic time, amount of radiographic contrast, and the number of catheters, guides, wires, balloons, and stents are important metrics that should be kept as low as possible. The use of IVUS to guide PCI does not cause any significant increase in any of these parameters when compared to conventional angiography-driven PCI.

FUTURE GOALS:
FORWARD-LOOKING IVUS

Limitations of current IVUS probes encourage development of smaller IVUS probes along with the design of forward-looking probes. The development of captive micromachined ultrasonic transducers has given a glimpse at the hopeful future of forward-looking IVUS. This thin, small-diameter, disc-like array of transducers allows for volumetric images at frequencies that allow for intracoronary imaging. The unique design of the membrane tip allows flexibility to change frequencies within the coronary artery. Lower frequencies can be employed for conventional higher penetration images useful for guidewire placement. Collapsing the array allows for higher frequencies, which provides high-resolution diagnostic images. Additional enhancements are technologies that include incorporation of tissue harmonic imaging, which may provide more enhanced intracoronary resolution, as well as the ability to detect microbubbles with subharmonic imaging allowing vasorum and molecular imaging. Although still in the initial phases of development for coronary imaging, this technology stands on the exciting horizon of forward-looking IVUS for coronary imaging.
CONCLUSION

IVUS has been well described for use in routine evaluation of coronary artery disease and plaque analysis. IVUS has been shown to be a powerful asset in accomplishing successful recanalization of CTOs. Employing IVUS in branching vessel disease, true and false lumen detection, and as a guide to salvage a failed revascularization attempt clearly demonstrates its usefulness for CTOs. The ultimate use of IVUS rests in its ability to evaluate disease extent and vessel size and to guide proper balloon and stent selection to maximize lumen gain in these complex scenarios. Technologic advances promise to open doors to techniques that will further improve rates of successful intervention of CTOs.

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