

Recent Progress of the Use of Interventional Therapy for Chronic Total Occlusion

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ABSTRACT

Chronic total occlusion (CTO) remains one of the most challenging lesion subsets for interventional cardiologists due to a low success rate and higher incidence of restenosis, especially with current use of bare metal stents (BMSs). However, successful CTO revascularization has a beneficial effect on long-term survival and relief of angina. With recent advances in technology (with the use of special techniques and devices), the initial success rate of recanalization of occlusions is quite high (approximately 90%). However, the long-term clinical outcome of the use of bare metal stents is not satisfactory due to a high restenosis rate. Recently, the introduction of the sirolimus-eluting stent (SES) and paclitaxel-eluting stent (PES) has shown favorable clinical outcomes, such as a reduction in the restenosis rate in patients with CTOs. Consequently, the use of the new types of stents can reduce the incidence of major adverse cardiac events detected at follow-up. (**Korean Circ J 2008;38:295-300**)

KEY WORDS: Coronary occlusion; Angioplasty; Drug-Eluting stents.

Introduction

Chronic total occlusion (CTO) of coronary artery disease is defined as total occlusion with either a known duration of more than three months or the presence of bridging collaterals. The long-term success after percutaneous coronary intervention (PCI) for CTOs is hampered by high rates of subacute reocclusion and late restenosis. After successful recanalization of total occlusion (provided the vessel remains patent), patients report relief from symptoms and develop improvement of left ventricular function, have fewer cardiac events and have fewer requirements for bypass surgery.^{1,2)} In addition, several randomized trials have demonstrated that stent implantation decreases the rate of restenosis and reocclusion³⁻⁹⁾ and confers a long-term survival advantage.¹⁰⁾ However, restenosis had remained the major complication that has limited the late outcome after PCI prior to the introduction of drug-eluting stents (DESs). Since 2002, DES has been available in Asian countries and there have been several reports about the efficacy of DESs for the reduction of restenosis after DES implantation, and the reports have described a dramatic reduction of restenosis¹¹⁻¹⁵⁾ as compared with the use of

bare metal stents (BMSs). Another obstacle of PCI for CTO is technical difficulty to recanalization of CTOs. With recent advanced in technology (special techniques and devices) and increased operator experience, the initial success rate of opening occlusions reached quite high percentage (around 90%), so we have much higher success rate of recanalization of CTOs and much lower incidence of restenosis. Has the time come to do more CTOs now?

Basic Knowledge of Chronic Total Occlusion Interventions

Consideration of the pathological features of CTOs, assessment of the difficulty of treatment of CTOs based on angiographic findings (Table 1) and a strong consideration of the appropriate selection for the indication of CTO-PCI are very important to select a proper strategy to treat CTOs with the right materials during procedures and ultimately improve patient long-term clinical outcome. Furthermore, an appropriate access site (femoral and/or radial) should be considered based on the clinical condition of the patients (radial or femoral does not matter as a 6 Fr guiding catheter is an appropriate size in either case). Dual injection (simultaneous contralateral injection) should be performed to evaluate the length of the lesion, to use as a landmark of the target of PCI guide wire, and to use as a route of the

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Table 1. Factors influencing the success of CTO interventions

1. Severe calcification
2. Target vessel tortuosity
3. Unknown length of CTO
4. No visible stump
5. Presence of a bridging collateral
6. Long length of CTO

CTO: chronic total occlusion

Table 2. Characteristics of wires for chronic total occlusion

Manufacturer	Wire	Shaft and tip diameter	Tip stiffness, g
Guidant	High torque intermediate	0.014"	2-3
	Cross-it 100	Shaft 0.014"	2
		Tip 0.010"	
	Cross-it 200	Shaft 0.014"	3
	Cross-it 300	Tip 0.010"	
	Cross-it 400	Shaft 0.014"	4
		Tip 0.010"	6
Whisper	0.014"	1	
Boston scientific	Pt graphix and graphix P2	0.014"	3-4
	Choice PT and P2	0.014"	2
Asahi Intecc	Miracle brothers	0.014"	3,4,5,6 and 12
	Conquest and conquest pro	Shaft 0.014"	9 and 12
		Tip 0.009"	
	Fielder	Shaft 0.014"	1
	X-treme	Shaft 0.014"	0.8
Tip 0.009"			
Johnson and Johnson	Shinobi	0.014"	2
	Shinobi plus	0.014"	4

retrograde approach. In addition, selection of an appropriate guiding catheter (a back-up catheter is usually required) is important to provide safe access of the interventional tool (e.g., guide wire, balloon, stent). If additional back up of the guiding catheter is required, several techniques to stabilize the catheter should be used. Finally, the most important selection of a CTO tool is guide wire selection. A guide wire should be selected based on each condition of a CTO. Recently, several manufacturers have developed special guide wires dedicated for the treatment of CTOs.

Recent Progress of Chronic Total Occlusion Intervention Devices

Guide wires

This step is a specific major feature of CTO PCI. Recently some physicians have recommended the use of a special guide wire combining the hydrophilic tip of the guide wire and slightly stiffer body of the guide wire to improve tracking in the CTO lesion. The CTO guide wire itself has to penetrate the proximal edge to

advance in the core of the CTO lesion with avoidance of subintimal tracking and finally has to be localized in the distal true lumen. The guide wire should have "stiffness, steerability and slipperiness" inside the CTO lesion. However, as there is no perfect CTO guide wire, it is most important to select an appropriate wire for each CTO condition. The mechanical characteristics of the wires are described in Table 2.

Hydrophilic wires (Whisper, Fielder, X-treme)

Hydrophilic wires are rarely used in case of CTO intervention as these wires can penetrate easily into the subintimal space without tactile feedback. The only exception is a hydrophilic soft wire such as the Whisper and Fielder wire in case of CTO lesions with a straight micro-channel (functional total occlusion). Recently, some physicians have recommended the use of hydrophilic wires to trace the very small channel inside the CTOs.

Non-coated coil wires (Conquest, Miracle brothers, others)

Non-coated coil wires tend to advance straight with more resistance inside the CTO (especially the Miracle Brothers and the Conquest guide wires), which have exceptional torque response even within a fibro-calcified CTO. A non-lubricated wire is important especially when attempting to penetrate the distal fibrous cap of a CTO. Thus, lower-force wires are generally initially used (e.g. Intermediate, Miracle Brothers, 3g) and if highly calcified lesions are encountered, the guide wire should be substituted with a more powerful, stiffer guide wire that is suitable for each situation of a CTO lesion.

Wires for retrograde approach (Fielder, X-treme)

The retrograde approach for CTO is relatively new trend, especially in cases where the left anterior descending (LAD) septal channel is used. Once retrograde wiring succeeds through the septal channel, recanalization of the CTOs can succeed with a high success rate. However, the size of the septal channel is quite small with some tortuosity, and steep angled bending is present that is close to the distal right coronary artery (RCA). Thus, guide wires for the retrograde approach require a micro-tube catheter support and should be a hydrophilic wire such as the Fielder and X-treme wire to negotiate the tortuous and small vessel. After successful passage of the wire and micro-catheter through the collateral channel into the target vessel, the guide wire should be changed to a stiffer wire to open the CTO in a retrograde manner.

Tornus catheter system

The Tornus catheter (Asahi Intecc, Aichi, Japan) was developed as a novel penetration catheter for severely tight stenotic coronary lesions. The outer diameter is 0.70 mm (2.1 Fr). The inner diameter is 0.46 mm and is suitable for a 0.014 inch guide wire. Since the coil is

stranded with eight stainless wires and a length of 150 mm from a tapered tip, the Tornus catheter has desired flexibility and torquability.

It can cross through severe stenosis easily with a counterclockwise rotation along the guide wire because the shaft is stranded clockwise. If the tip of the catheter does not advance through the lesion by manipulation, it is sometimes required to release the catheter from rotational force in order to avoid breakage of the shaft. Due to the severe hardness inside the CTO, the Tornus catheter is used to make a small track in the CTO lesion, resulting in successful delivery of a balloon catheter and stent system to the lesion.

Recent Progress of Chronic Total Occlusion Intervention Techniques

Stabilization of the guide catheter

It is very important to select an appropriate guide catheter (basically, a strong back-up catheter is better) not only for crossing the CTO lesions by the guide wire but also for delivering the several devices after recanalization of the lesions. However, occasionally the guide catheter backs out as the wires or devices are advanced, and the guide has inadequate back up. Thus, it is sometimes necessary to stabilize the guide catheter by another method. At first, the guide wire has to be repositioned by deep seating or use of a larger guide catheter. If additional back up of the guide catheter is required, the use of the anchor wire technique and anchor balloon technique are needed to resolve situations using side branches with a wire alone or balloon inflation.

Troubleshooting techniques

At first, to enable maximal guide wire torquability and pushability, a micro-tube catheter should be regularly used. An appropriate guide wire for each CTO condition is then selected; however, the selection process is very difficult and there is no straightforward selection procedure. Generally, torquability is proportional to the hardness of the wire tip of the guide wire, but with a harder wire less resistance is felt at the tip by the operator, and there is a higher risk of creating a false lumen and less ability to negotiate bending in the CTO lesion. After selection of the first guide wire, the wire has to penetrate the CTO lesion and advance to the core of occlusion while avoiding progress in the subintimal pathway and hopefully cross the distal edge of the lesion. If there is a difficult situation during this procedure, it is necessary to change the guide wires and to use several special techniques to solve the situation.

Parallel wire technique

When a guide wire is repeatedly advanced into the subintimal space, it can be left to use as a landmark to

avoid the new wire protruding in the same space that easily causes collapse of the distal true lumen. Then, a second wire is advanced through a micro-tube catheter in order to avoid twisting the two wires. A modification of this technique called the “seesaw wiring method” provides the alternate use of two guide wires to double the chance to place the wires in the distal true lumen. The effectiveness of the parallel wire technique is the following. (1) The first wire can occlude the entry site of the false lumen and can be used as a landmark (with the potential to reduce the contrast). (2) The first wire can modify the arterial geometry, resulting in a reduction of the resistance for the second wire passage. (3) The second wire can find the true lumen easier than the first wire using the first wire as a landmark. In this situation, the tapered-tip wires are considered more adequate for the second wire than the conventional wires as they can create a channel difference from the channel created by the first wire owing to the stiff and tapered tips.

Intravascular ultrasound-guided wiring technique

The IVUS-guided wiring technique is a useful strategy, especially for the detection of the entry site of the CTO. For these cases, and if the branch is large enough to advance an IVUS catheter, the IVUS catheter can pinpoint the central area of the main lumen at the beginning of the CTO lesion. Furthermore, IVUS can provide information such as the best position of the wire entry point and can check the location of the wire in the CTO lesion.

Retrograde approach technique

Recently, the retrograde approach has been introduced using a septal collateral channel to treat RCA or LAD CTO, especially, when antegrade crossing of a CTO fails.¹⁶⁾ The basic concept of the retrograde approach is shown in Figure 1. In this technique, the operator utilizes the existence of clear visibility and continuous septal connected straight collaterals that is a shorter route to the recipient vessel, and has a less tortuous anatomy as demonstrated by bilateral injection angiography. Careful selection of the guiding catheter is necessary, as a supportive and short guide catheter (90 cm) should be used to enable a longer coronary segment to pass through. The hydrophilic soft wire with support micro-tube catheter is necessary to advance through the collateral with the retrograde approach of the CTO. This technique is used for long RCA and LAD CTOs, in which the retrograde wire is navigated through a septal branch. Once these wires advance into the target recipient, the wire should be advanced in the antegrade guide catheter or aorta.

The retrograde wire is easily trapped in the guide catheter by a PCI balloon to provide large back-up support to advance the small size balloon retrogradely and dilate

the CTO lesion. After dilatation of CTO lesion, the antegrade wire is localized in the distal true lumen easily with an antegrade manner by proceeding along the retrograde wire that is already passed to the proximal vessel. If the retrograde guide wire cannot enter the inside of the target vessel, the controlled antegrade and retrograde subintimal tracking (CART) technique should be used.¹⁷⁾ In these situations, it is very important to minimize the enlargement of the subintimal space at the CTO site; therefore, the CART technique is introduced. The basic concept of the CART technique is that once the retrograde guide wire penetrates from the distal true lumen into the CTO lesion of the subintimal space, a small size balloon is advanced over the retrograde wire, and balloon to make a large crack. Consequently, the antegrade wire is advanced into the subintimal space easily, and eventually the antegrade wire easily localizes in the distal true lumen (Fig. 1).

Recent Progress of Clinical Data for Chronic Total Occlusion Intervention With the Use of Drug-Eluting Stents

The long-term success after PCI for CTOs is hampered by high rates of subacute reocclusion and late restenosis. Several randomized trials have demonstrated that stent implantation decreases the rates of restenosis and reocclusion, and confers a long-term survival advantage, even with use of bare metal stents. However, restenosis remains a major complication limiting late outcome after PCI. The use of DESs has proved to decrease restenosis (Table 3 and 4) in patients with CTOs and has also been shown to improve long-term clinical outcome. A lower success rate and higher restenosis rate of PCI for CTOs is a goal for interventional cardiologists. However, with the use of drug-eluting stents,

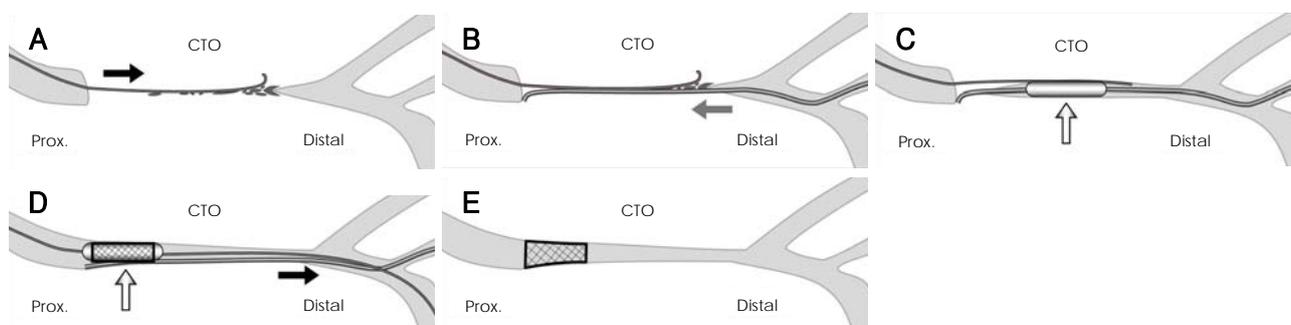


Fig. 1. Concept of the Retrograde Approach. A: the antegrade wire is unable to localize in the distal true lumen. B: the retrograde approach: the retrograde wire arrives from the distal collateral root to enter the CTO lesion. C: ballooning in a retrograde manner. D: re-wiring in an antegrade manner, followed by stenting. E: after stenting. CTO: chronic total occlusion.

Table 3. Follow-up results after sirolimus-eluting stent implantation for CTOs

	Migliorini et al. ¹⁸⁾	Hoye et al. ¹⁹⁾		Suttorp et al. ²⁰⁾		Jang et al. ²¹⁾	Nakamura et al. ²²⁾
Number	104	56		100		107	60
Follow-up period	6 months	6 months		12 months		12 months	12 months
MACE (%)							
Death	2.2	0		0		0	0
Q-MI	0	1.8		2		0	0
CABG	-	0		1		1.8	0
Re-PCI	7.6	9.1		4		1.8	3.3
Follow-up angiogram		Proximal 5 mm	In-stent	Distal 5 mm	In-stent		In-segment
Reference diameter (mm)	-	3.02 ± 0.53	2.46 ± 0.81	2.12 ± 0.83	3.44 ± 0.54		2.9 ± 0.5
MLD (mm)	-	2.33 ± 0.90	1.91 ± 0.68	1.81 ± 0.75	-		2.09 ± 0.73
Late loss (mm)	-	0.10 ± 0.80	0.13 ± 0.46	-0.86 ± 0.54	0.05 ± 0.81	-0.07 ± 0.72	0.4 ± 0.8
Restenosis (%)	19.2	9.1		7		11	9.4
Reocclusion (%)	11.5	30		4		0	0
Comparison with control (BMS)							
Reocclusion (%)	18.5	-		13.0		-	5.8
Restenosis (%)	45.0	-		41.0		-	31.7

CTO: chronic total occlusion, MACE: major adverse cardiac effect, Q-MI: Q wave myocardial infarction, CABG: coronary artery bypass graft, Re-PCI: re-percutaneous coronary intervention, MLD: minimal luminal diameter, BMS: bare metal stents

Table 4. Follow-up results after paclitaxel-eluting stent implantation for CTOs

	Werner et al. ²³⁾	Buellesfeld et al. ²⁴⁾	Jang et al. ²¹⁾	
Number	48	45	29	
Follow-up period	12 months	6 months	12 months	
MACE (%)				
Death	0	0	3.4	
Q-MI	0	0	0	
CABG	0	0	0	
Re-PCI	6.3	15.6	0.9	
Follow-up angiogram		In-stent	In-segment	
Reference diameter (mm)	2.57 ± 0.47	2.92 ± 0.51	2.90 ± 0.51	3.1 ± 0.4
MLD (mm)	2.05 ± 0.59	2.02 ± 0.78	1.78 ± 0.80	2.0 ± 0.9
Late loss (mm)	0.19 ± 0.62	0.26 ± 0.55	0.13 ± 0.58	-
Restenosis (%)	2.1	-	-	-
Reocclusion (%)	8.3	18	-	28.6
Comparison with control (BMS)				
Reocclusion (%)	23.4	-	-	-
Restenosis (%)	51.1	-	-	-

CTO: chronic total occlusion, MACE: major adverse cardiac effect, Q-MI: Q wave myocardial infarction, CABG: coronary artery bypass graft, Re-PCI: re-percutaneous coronary intervention, MLD: minimal luminal diameter, BMS: bare metal stents

there is a high success rate and a considerable lower restenosis rate after PCI for CTOs. Therefore, the time has now come to perform a PCI for CTOs as a routine procedure by interventionists, and all interventional cardiologists will require the basic skills of CTO intervention in the near future.

Conclusion

With recent advanced special techniques and devices, such as dedicated CTO guide wires and the Tornus system (devices) and the parallel wiring technique, IVUS-guided wiring technique, retrograde wiring approach (techniques), the initial success rate of PCI for CTO is high (approximately 90%).

According to the several emerging studies that have evaluated the efficacy of drug-eluting stent implantation after successful recanalization of CTOs, the use of drug-eluting stents enhances definitely the long-term clinical outcomes after PCI for CTOs.

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