OUTCOMES

The mean follow-up time was 51±27 months. In category 1 (PSVR<2.00), Kaplan-Meier analysis estimates for primary patency rates were 62.6%, 36.8%, and 27.6% for one, five, and seven years, respectively. In category 2 (PSVR<2.40), the estimates were 75.2%, 46.5%, and 37.1% for one, five, and seven years, respectively. In category 3 (PSVR<2.85), the estimates were 75.2%, 46.1%, and 46.1% for one, five, and seven years, respectively **(Figure 1)**.

A significant difference in primary patency was observed between categories 1 and 3 (p=0.038, log-rank test). No difference was observed between categories 2 and 3 (p=0.786, log-rank test), and a trend for differences was observed between categories 1 and 2 (p=0.069, log-rank test).

Discussion

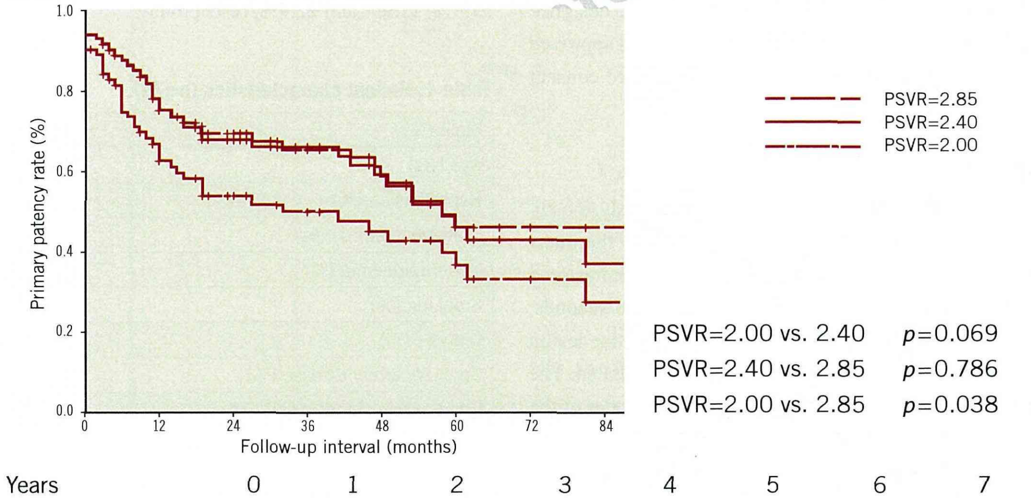
The use of EVT for lower extremity ischaemia has become widespread because of technological advances, and the strategy of revascularisation has shifted from surgical treatment towards EVT[6-9]. Considerable advances in EVT technology for SFA disease include the dramatic increase in the use of nitinol stents, which have become the standard of care to date because of the results obtained from randomised trials[10,11].

Recently, many trials have been conducted on SFA stents, and some of these trials have been completed. We were able to select new-generation stents based on the results of these trials. When interpreting the results of recent SFA studies, we must consider the PSVR definitions used by each study. To clarify this confusion regarding PSVR definitions, we have conducted this study. There are conflicting data regarding the benefits of femoral stenting. Many studies are currently in progress to examine the use of other self-expanding stent platforms for patients with intermittent claudication and rest pain. However, each of these trials uses their own PSVR definition for the evaluation of the patency rate. In this report we show the impact of changing PSVR thresholds on the patency rates of SFA.

We have to do a rethink on the optimal PSVR to detect restenosis, but the problem with evaluating restenosis is that its definition is different in each trial. This could be the basis of confusing results in terms of the patency rate for each stent. However, each stent design has a different stiffness, which may influence the PSVR.

Study limitations

This was a retrospective study. The number of patients followed in the chronic phase was relatively small. This study might lack



Years		0	1	2	3	4	5	6	7
At risk	PSVR 2.0	83	43	31	24	19	12	6	4
	PSVR 2.4	83	52	41	32	26	14	7	5
	PSVR 2.8	83	52	42	32	26	14	7	5
%	PSVR 2.0	100	62.6	53.8	49.9	45.3	36.8	33.1	27.6
	PSVR 2.4	100	75.2	67.9	66.0	59.4	46.5	43.2	37.0
	PSVR 2.8	100	75.2	69.3	65.6	58.9	46.1	46.1	46.1
SE	PSVR 2.0	0.000	0.055	0.058	0.060	0.063	0.068	0.070	0.077
	PSVR 2.4	0.000	0.050	0.055	0.056	0.062	0.071	0.073	0.085
	PSVR 2.8	0.000	0.050	0.054	0.057	0.063	0.071	0.071	0.071

Figure 1. *The primary patency between categories 1 and 3 (p=0.038, log-rank test) was significantly different. No difference was observed between categories 2 and 3 (p=0.786, log-rank test), and a trend for differences was observed between categories 1 and 2 (p=0.069, log-rank test). SE: standard error.*

statistical power to confirm the differences between groups. Further investigation of new-generation stents is needed in the near future.

Conclusion

When we compare trials for the purpose of selecting a new stent that has a better patency rate with less restenosis, we should consider the definition of restenosis in each of the trials that we are examining.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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◆ENDOVASCULAR THERAPY REVIEWS ◆

Contemporary Crossing Techniques for Infrapopliteal Chronic Total Occlusions

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The synergism of technical refinement and advanced technology has significantly increased the popularity of infrapopliteal intervention. Since chronic total occlusion (CTO) is a common disorder among patients with symptomatic infrapopliteal artery disease, infrapopliteal CTO intervention is now evolving rapidly in the field of endovascular intervention. Guidewire crossing through the CTO is essential for a successful procedure. We review up-to-date infrapopliteal CTO crossing techniques based on the current literature.

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Key words: infrapopliteal artery disease, chronic total occlusion, endovascular technique, crossing device, recanalization device

The synergistic interaction of technical refinement and advanced technology has achieved acceptable clinical outcomes of infrapopliteal intervention during the past decade.[1,2] In particular, the advent of drug-eluting stents and drug-coated balloons has the potential to decrease the restenosis rate and the need for clinically-driven repeat intervention, expanding the performance of complex infrapopliteal intervention.[3–6] Given the frequency of chronic total occlusion (CTO) in the lesion morphology of patients with critical limb ischemia (CLI),[7] techniques for infrapopliteal CTO interventions are evolving rapidly. Since manipulating a guidewire across the CTO is essential for a successful procedure, a variety of crossing techniques have been developed and are discussed in this up-to-date review.

CTO CROSSING METHODS

Successful antegrade or retrograde CTO crossing involves distinct stepwise procedures (Fig. 1, Table) that can track in the intraluminal or subintimal space in either direction and with each type of technique. Thus, different scenarios can be observed during the passing of infrapopliteal CTO lesions (true-to-true, true-to-false-to-true, etc.).

Fundamental System and Guidewire Knowledge

The most standard system for infrapopliteal CTO intervention is the use of a 0.014- or 0.018-inch guidewire through an over-the-wire balloon catheter (1.5 to 2.0 mm in diameter and 4 to 10 mm long), an end-hole

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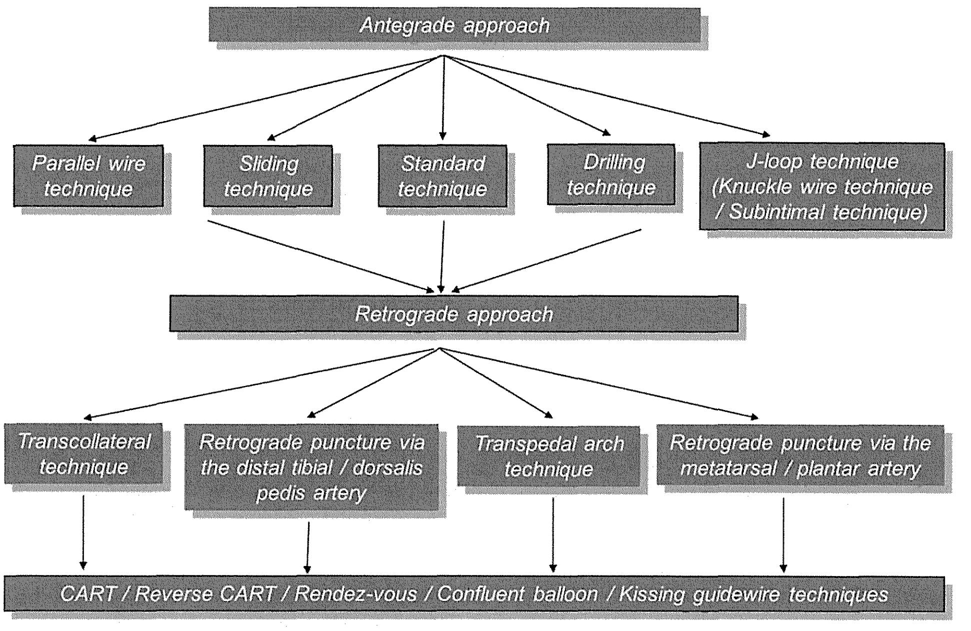


Figure 1 ◆ Steps involved in infrapopliteal CTO crossing techniques.

microcatheter, or a 3- or 4-F multipurpose catheter. The over-the-wire technique increases wire maneuverability, simplifies frequent wire exchanges or tip shaping, and increases backup force. When negotiating a CTO in the bifurcations, an angled tip 3- or 4-F JR or Venture catheter (Vascular Solutions Inc, Minneapolis, MN, USA) or a dual lumen device for bifurcation use (Crusade; Kaneka Medics, Osaka, Japan) can provide the coaxial alignment necessary to cross the occlusive lesion.[8] Each guidewire and catheter combination has inherent advantages and disadvantages when used for crossing CTOs. It is crucial for interventionists to appreciate the characteristics of these devices and become familiar with a couple of them for daily use.

There are primarily two types of CTO guidewires: hydrophilic and non-hydrophilic. In the field of infrapopliteal CTO intervention, hydrophilic guidewires are favored due to their minimal resistance and increased lubricity, despite the limited tactile feel and increased likelihood of inadvertently entering false channels. Non-hydrophilic guidewires may be more controllable and provide better tactile feel, but they tend to encounter more resistance inside CTO lesions. Most of the currently available guidewires have a hydrophilic coating. Also, a variety of guidewires with 0.8 to 90 g tip loads are available, and guidewires can be further divided into those with non-tapered tips (0.014- or 0.018-inch) and those with tapered tips (0.008- to 0.010-inch, 0.013-inch). The penetration power is another important index with regards to passing CTOs. It can be calculated using the following formula: tip load $\div$ [3.14 $\times$ (tip diameter/2)^2]. Figure 2 offers an assortment of guidewires of varying tip loads and penetration powers that are available in Japan; the information can be used to identify similar guidewires in the reader's country.

Antegrade Techniques

With respect to arterial access, the antegrade approach requires ipsilateral antegrade femoral access for use with shorter devices and higher performance levels of pushability, torqueability, crossability, or trackability.[9] Using a long sheath that extends down to the level of the popliteal artery cannot only increase these advantages but also reduce the use of contrast. Deep engagement of a long sheath into the crural arteries, which can be coaxially achieved at the time of balloon deflation, can provide more backup force in

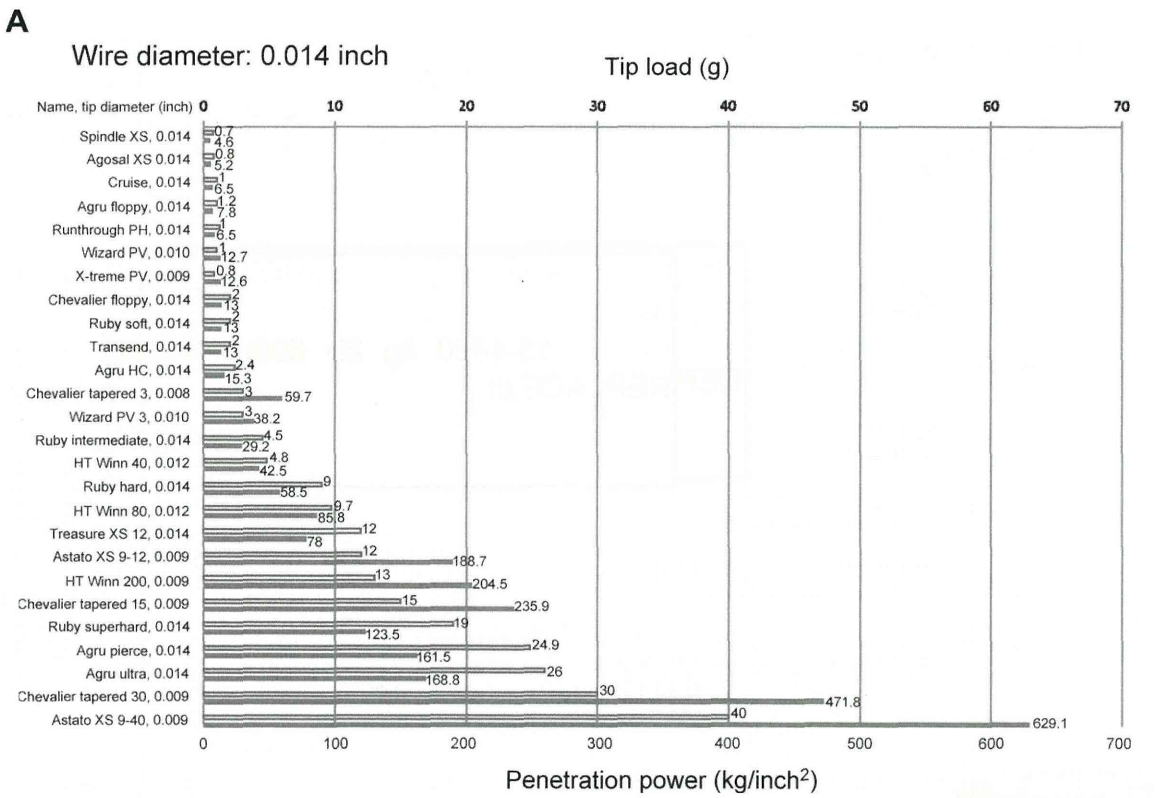
TABLE
Characteristics of Antegrade or Retrograde Crossing Techniques

Technique	Indication	Advantages	Disadvantages
Antegrade			
Standard/sliding	Softer and less calcified lesion, microchannel, or subtotal lesion	Less traumatic.	Possible low success rate, not suitable for hard lesions.
Drilling	*Short segment occlusion*	*High chance of* intraluminal crossing.	*Not suitable for long* occlusions or complex cases. Modulating the strength of the drilling motion limits the risk of perforation, but also limits the chance of success.
Penetration	Hard or calcified lesion, reentry from the subintimal space into true lumen	Increases the success rate of antegrade crossing.	Potential risk of vessel perforation.
Parallel wire	Any situation	Increases the success rate of antegrade crossing.	Need for multiple guidewires.
Knuckle wire, loop, subintimal angioplasty	Long occlusion	Rapid traversal of long total occlusions, less likely to cause vessel perforation.	Risk of compromising branches or being stuck in the calcified lesion. Potential failure of reentry into the true lumen.
Retrograde			
Distal tibial or dorsalis pedis artery puncture	Preserved distal vessel	Stronger backup force to cross the lesion.	Potential risk of puncture site occlusion during the procedure or during follow-up.
Transcollateral	Unavailable reconstituted vessel and sufficient collateral vessel	No need for retrograde puncture.	Insufficient backup force. Potential risk of injury to the collateral vessel.
Transpedal arch	No distal vessel available	Possibility of complete revascularization.	Potential risk of compromising branches in the foot and injury of the pedal arch. Insufficient backup force.
Metatarsal or plantar artery puncture	Occlusion of the pedal arch	Possibility of revascularization of the dorsalis pedis artery or plantar artery.	Failed procedure resulting in urgent worsening of underlying toe ischemia.
CART, reverse CART, rendezvous, confluent balloon, kissing wire	Failed reentry using conventional techniques	Increases the success rate of guidewire crossing.	Need for further dedicated devices.

CART: Controlled antegrade and retrograde tracking.

the treatment of severely calcified or hard lesions.

Standard Technique / Sliding Technique. Infrapopliteal CTO intervention can take advantage of standard coronary CTO techniques. The initial approach for CTOs is the use of a 0.014-inch hydrophilic or non-hydrophilic guidewire through an over-the-wire system. In particular, soft tip hydrophilic guidewires with an ~1-g tip load [for example, non-tapered 0.014-inch: Cruise (Asahi Intecc, Aichi, Japan); tapered 0.010-inch: Wizard PV

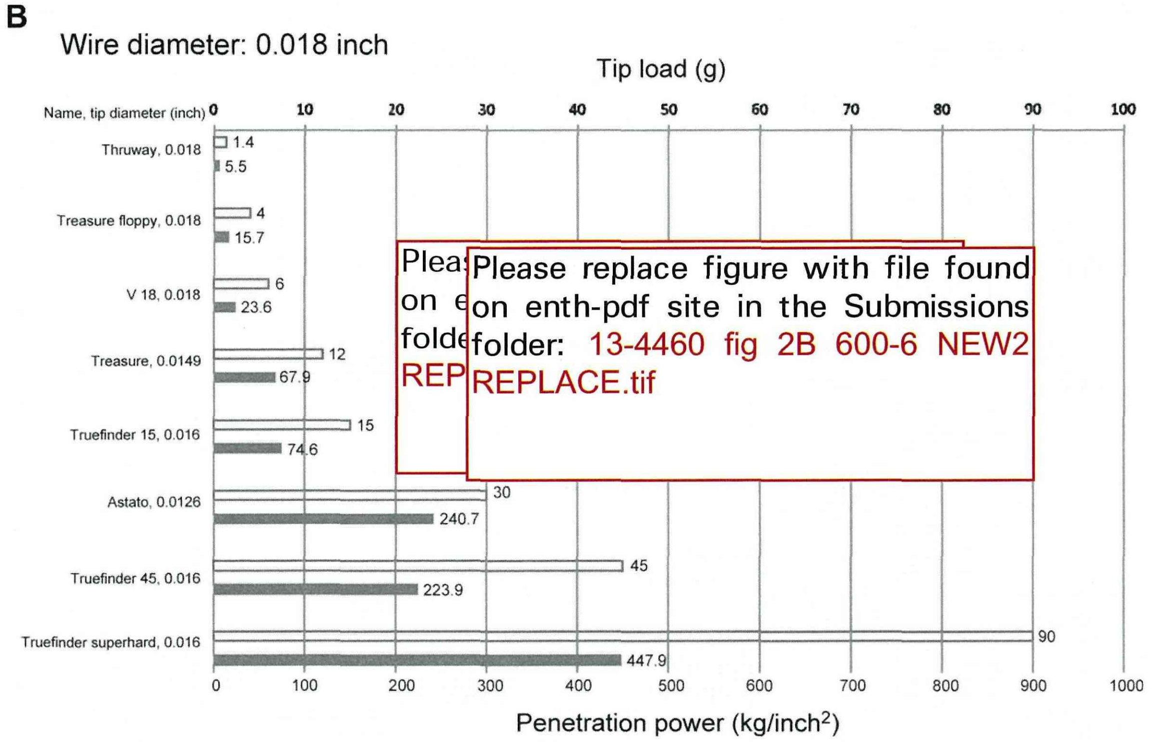


◆ **Figure 2A** There is a wide variety of (**A**) 0.014-inch guidewires in Japan in terms of tip load and penetration power. Most of the guidewires have a hydrophilic coating, except for Agru floppy, Agru ultra, and Agru pierce. The white bar indicates tip load and the black bar indicates penetration power. Note that penetration power varies independently of tip load. This information can be used to find similar equipment in the reader's country.

(Japan Lifeline, Tokyo, Japan)] can be used in the standard or sliding technique because of their inherent ability to negotiate soft lesions, microchannels, or subtotal occlusive lesions.[10] A specialized 0.010-inch soft guidewire with a tapered tip (e.g., Wizard PV or X-treme PV) may also increase the likelihood of selecting microchannels (Fig. 3).

Drilling Technique. When attempting to negotiate a hard lesion, such as a fibrous or calcified cap of a CTO, drilling with an active rotation and pecking motion using stiff wires with an ~10-g tip load [Ruby hard (Kaneka Medics), HT Winn 40 (Abbott Vascular, Santa Rosa, CA, USA), Treasure XS12 (Asahi Intecc), etc.] is essential due to the greater tactile feel of the torque response (Fig. 4A). As with coronary CTO intervention, a 40° to 60° bend ~1 to 2 mm from the wire tip can be made. For hard lesions, balloon dilation could yield further advancement of the guidewire due to a stronger backup force (Fig. 4B). This technique is indicated for relatively short segment CTOs (Fig. 4C–E). Since Kawarada et al.[11] initially reported CTO recanalization of the dorsalis pedis artery using CTO-dedicated 0.014-inch guidewires, this technique has been applied even to below-the-ankle CTOs, but it is not suitable for complex lesions, including long or calcified lesions.

Parallel Wire Technique. This technique, which was developed for coronary CTO intervention, is also called the "seesaw technique" by Japanese coronary CTO masters when over-the-wire balloons are employed.[12] When the first guidewire has been advanced into a false lumen, the technique can be one option for successfully crossing the lesion with a minimal risk of extensive subintimal dissection and perforation. By leaving the first



◆ **Figure 2B** (B) The variety of 0.018-inch hydrophilic guidewires manufactured in Japan. The white bar indicates tip load and the black bar indicates penetration power. Note that penetration power varies independently of tip load. This information can be used to find similar equipment in the reader's country.

guidewire in place as a marker in the subintimal space, a stiff second guidewire can be used to probe the occlusion and get close to the true lumen. Repeated attempts to manipulate the guidewires open an opportunity to successfully enter the true lumen (Fig. 5).

Penetration Technique. The tip of a dedicated guidewire for penetration might require a penetration power of 100 kg/inch^2 or more, as well as a tip load of 10 g or more [Astato XS9-12 (Asahi Intecc), HT Winn 200T (Abbott Vascular), Ruby superhard (Kaneka Medics), etc.], although the lower tip resistance of such guidewires can make it easier for them to enter the subadventitial space and cause vessel perforation. In cases when it is difficult to enter the proximal fibrous cap due to hard plaque or thrombus, using the penetration technique with a slightly bent dedicated CTO guidewire is required (Fig. 6A). Since it might be difficult to appreciate whether the tip has engaged a true or false lumen as the guidewire becomes stiffer, these guidewires may be exchanged with soft guidewires following successful penetration. Also, as in cases of failed reentry from the subintimal space to the true lumen, possibly due to a hard or calcified distal cap, the penetration technique with a 0.014- or 0.018-inch dedicated CTO guidewire facilitates reentry into the true lumen (Fig. 6B–D).

Subintimal Angioplasty Technique (Knuckle Wire Technique, J-Loop Technique). In 1989, Bolia et al.[13] rediscovered a practical use for subintimal angioplasty, which was invented by Dotter in 1964,[14] and applied to the treatment of femoropopliteal occlusions. Since then, this technique has been extensively used to treat CTOs in the infrapopliteal arteries.[15] In the field of coronary CTO intervention, Colombo et al.[16] called this technique "subintimal tracking and reentry (STAR)." A modified STAR technique called "contrast-guided STAR" by Carlino et al.[17] could be helpful for visualizing the dissection plane with subintimal contrast injection. Currently, the subintimal angioplasty technique is also referred to as the "J-loop technique" or

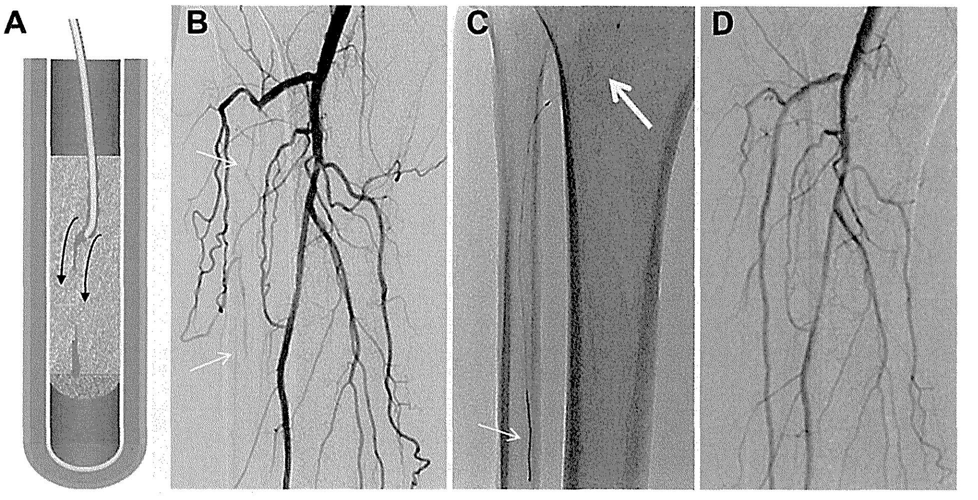


Figure 3 ◆ (**A**) Illustration of the sliding technique, which utilizes a 0.014-inch hydrophilic guidewire or a specialized 0.010-inch guidewire to explore microchannels or subtotal occlusions. (**B**) Baseline angiogram showing a likely microchannel or subtotal occlusion between tandem occlusions in the right anterior tibial artery (arrows). (**C**) The lesion was crossed using a combination of 0.010- and 0.014-inch guidewires (small arrow) supported by an over-the-wire balloon catheter (large arrow). (**D**) Excellent results after balloon angioplasty. A color version is available online at *www.jevt.org.*

"knuckle wire technique" (Fig. 7A,B) in the field of peripheral vascular intervention since this technique does not necessarily track in the subintimal space.[2,10,18] This technique is primarily indicated for long CTOs in the infrapopliteal arteries and could be beneficial if other revascularization approaches are not possible.

This technique can employ a 0.014-inch soft hydrophilic guidewire [e.g., Cruise (Asahi Intecc)] with the formation of a loop (J-tip configuration) to take advantage of the minimal resistance of the guidewire. Given the lack of tactile feedback, a soft 0.014-inch hydrophilic guidewire can be safely, reliably, and rapidly traversed down long CTOs in a

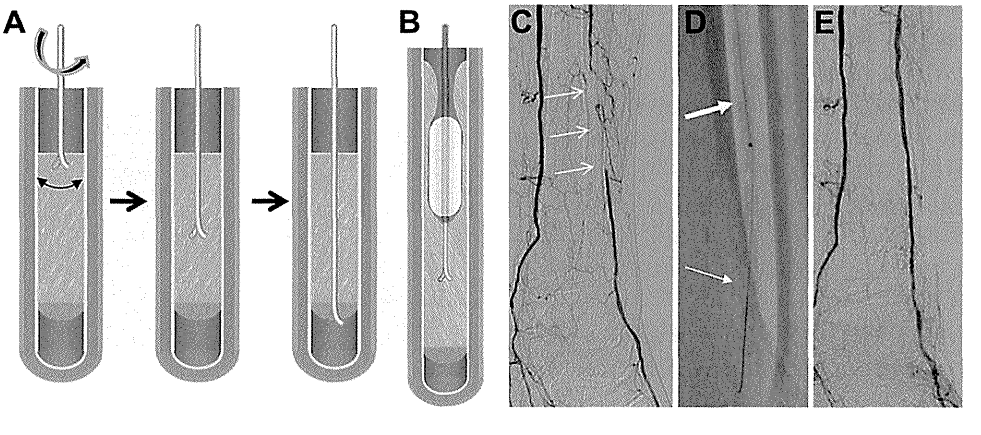


Figure 4 ◆ (**A**) Illustration of the drilling technique involving active rotation of the CTO-dedicated guidewire with a simultaneous pecking motion. (**B**) Balloon dilation for achieving a stronger backup force. (**C**) Baseline angiogram showing a short segment CTO in the left anterior tibial artery (arrows). (**D**) Successful crossing of the diffusely calcified vessel tract with the use of a CTO-dedicated guidewire (small arrow) supported by an over-the-wire balloon (large arrow). (**E**) Final angiogram showing an excellent result. A color version is available online at *www.jevt.org.*

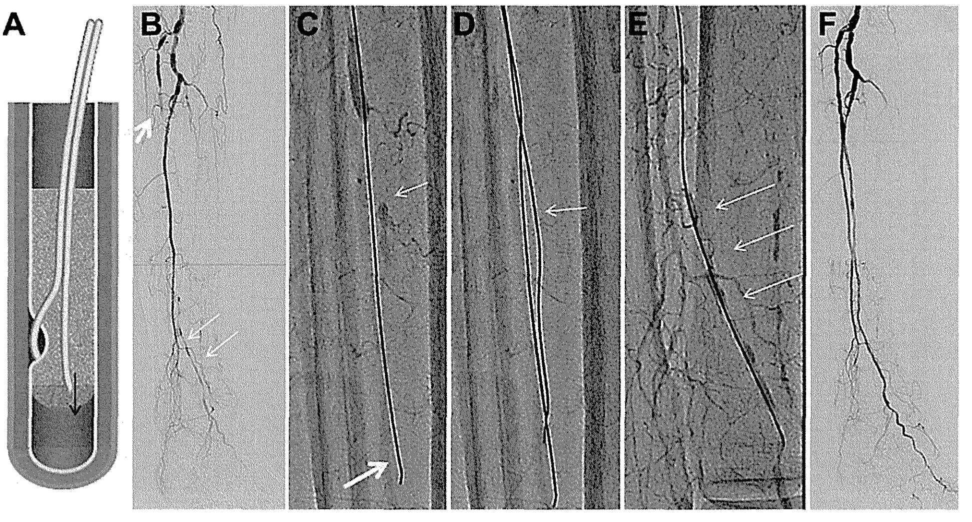


Figure 5 ◆ (**A**) Illustrations of the parallel wire technique. If the first guidewire enters a false lumen, it is left in place as a marker. A second guidewire can be used to probe the occlusion and redirect the first wire back into the true lumen. (**B**) Angiogram showing a CTO in the proximal segment of the right anterior tibial artery (large arrow) with the reconstituted vessel (small arrow). (**C**) The first guidewire entered a false lumen (large arrow). Note the reconstituted vessel on the left side of the first guidewire. (**D**) The second guidewire is advanced alongside the first guidewire (arrow). (**E**) Successful crossing of the second guidewire into the reconstituted vessel (arrows). (**F**) Final angiogram showing excellent revascularization after balloon angioplasty. A color version is available online at *www.jevt.org*.

true or false lumen. When tackling a hard lesion, the guidewire can be advanced with the assistance of a stronger backup force achieved by balloon dilation (Fig. 7C). Also, direct advancement of the over-the-wire balloon catheter or microcatheter in which the guidewire is accommodated might facilitate blunt crossing of the CTO (Fig. 7D). Stepwise advancement of the naturally formed guidewire loop (which may be knuckled or in the J-configuration) supported by an over-the-wire balloon can be very helpful until it spontaneously reenters the true lumen (Fig. 7E–I). In particular, serial balloon dilation of proximal lesions during this step-by-step approach can be of great help in decreasing catheter friction in tight CTOs.

Over 10 years ago, the technical success rate of subintimal angioplasty was ~80%. Vraux et al.[19] reported that the technical success rate was 78% (31/40 limbs) and Ingle et al.[20] reported 86% (60/70 limbs). Recently, this technique has been employed in the treatment of extensive tibial occlusions with below-the-ankle involvement.[21,22] Zhu et al.[22] employed this technique in 66 arteries in 57 limbs of 37 diabetic CLI patients with a technical success rate of 83.3% (55/66 arteries). Thus, this technique can be used as a standalone technique for infrapopliteal long CTOs, al-

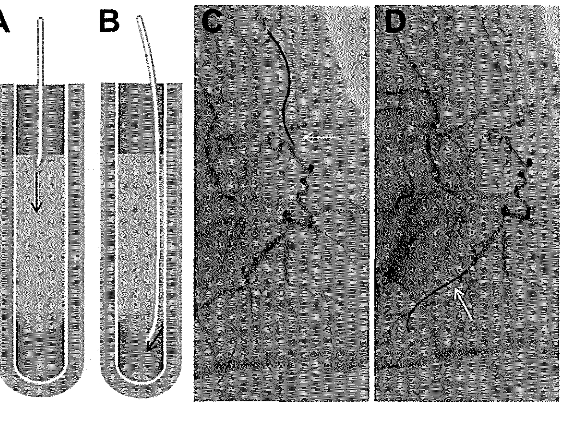


Figure 6 ◆ Illustrations showing the penetration technique being used with the (**A**) proximal and (**B**) distal hard caps. Note a slightly bent tip is used with this technique. (**C**) Angiogram showing the wire straying into the subintimal space (arrow). (**D**) The penetration technique facilitated reentry into the reconstituted plantar artery (arrow). A color version is available online at *www.jevt.org*.

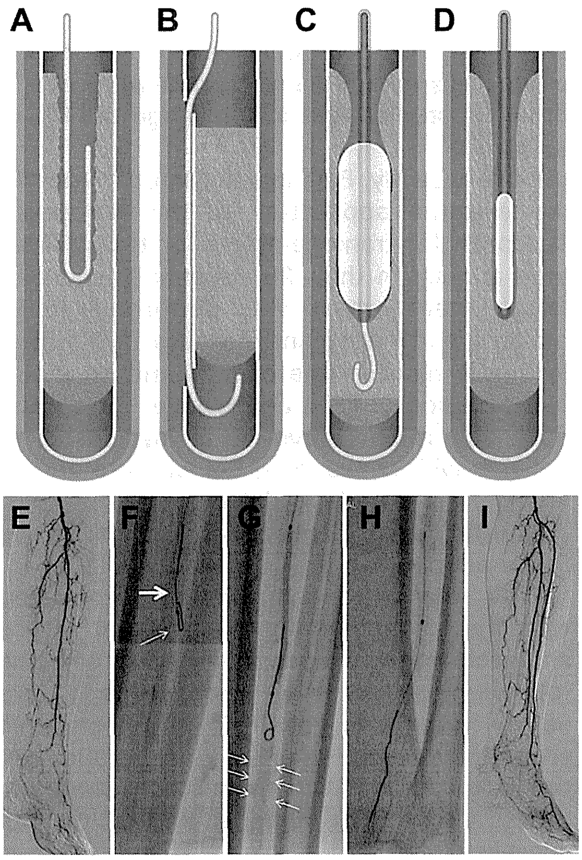


Figure 7 ◆ J-loop technique (knuckle wire or subintimal technique). (**A**) Blunt advancement of the hydrophilic or floppy guidewire in a J-loop configuration. (**B**) Subintimal tracking. Note spontaneous reentry beyond the distal cap. (**C**) Balloon dilation to obtain a stronger backup force with hard lesions. (**D**) Direct advancement of the balloon catheter with the guidewire inside. (**E**) Baseline angiogram showing a long CTO in the left anterior tibial artery. (**F**) Blunt advancement of a 0.014-inch guidewire in a J-loop configuration (small arrow) supported by an over-the-wire balloon catheter (large arrow). (**G**) Dilation of the over-the-wire balloon catheter was performed to obtain enough backup force to cross the hard lesion. Note the calcified tibial artery (arrows). (**H**) Step-by-step advancement of the guidewire facilitated successful crossing. (**I**) Final angiogram showing the establishment of one straight-line flow to the foot. A color version is available online at *www.jevt.org*.

though considerable precautions need to be taken in order to avoid compromising major branches with subintimal dissection, especially in the pedal arch. Also, a combination of the subintimal technique and other dedicated techniques, such as the penetration technique mentioned above, might yield higher rates of successful antegrade recanalization.

Retrograde Techniques

The retrograde technique can be considered after antegrade techniques have failed. The decision to use the retrograde technique requires careful assessment of wound healing and limb salvage considerations because procedure failure or complications could result in worsening of foot ischemia and catastrophic scenarios. Using a familiar combination of equipment, including needle, guidewire, and long supportive catheter ($\geq$80–100 cm), can result in a safe and reliable retrograde procedure. Even with the retrograde technique, an over-the-wire technique is mandatory, and similar consideration of guidewires needs to be undertaken.

Antithrombotic management is crucial because the diminished blood flow due to the sheath profile can carry the risk of thrombus formation and puncture site occlusion. Therefore sufficient heparinization (activated clotting time >200 seconds) is mandatory during the procedure. Also, since sheath placement (3- or 4-F) could pose a procedural hazard, a sheathless approach is recommended. However, retrograde sheath placement can be considered when a detailed retrograde sheath angiogram is required for better understanding of the distal segment and stronger backup force during retrograde crossing.

Retrograde Approach via the Distal Tibial or Dorsalis Pedis Artery. The concept of using a retrograde approach for infrapopliteal CTO recanalization originated from the case reports of Iyer et al.[23] in 1990. They described using a posterior tibial artery cutdown at the level of the ankle to treat occlusions in the tibioperoneal to posterior tibial arties in a primary attempt to treat flush occlusion in one case and a secondary attempt following unsuccessful antegrade crossing in another case.

In 2003, Botti et al.[24] reported that a retrograde approach was percutaneously attempted in 6 patients following failed antegrade crossing and was successful in all cases where the retrograde wire was snared from

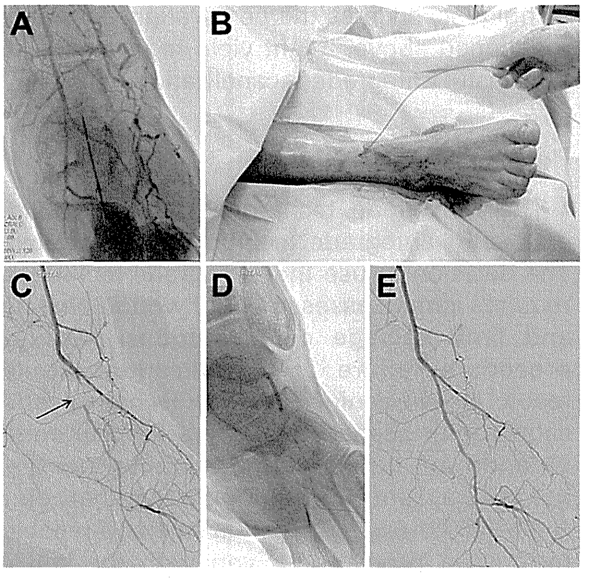


Figure 8 ◆ Retrograde approach and puncture site occlusion. (**A**) Fluoroscopically guided puncture of the dorsalis pedis artery. (**B**) Sheathless microcatheter placement. (**C**) Puncture site occlusion in the dorsalis pedis artery (arrow). (**D**) Recanalization of the puncture site occlusion by balloon angioplasty. (**E**) Endovascular repair was achieved.

the antegrade access site. In 2005, Spinosa et al.[25] described an antegrade-retrograde approach that they successfully implemented in all 21 of the limbs they treated; they called this antegrade-retrograde subintimal tracking technique SAFARI (subintimal arterial flossing with antegrade-retrograde intervention). Subsequently, antegrade-retrograde intervention was employed in cases involving failed antegrade reentry or an undetermined proximal occlusion stump (flush occlusion) in the setting of CLI. Retrograde puncture at the level of the ankle or foot or at the crural level can be performed under fluoroscopic guidance (Fig. 8A). Ultrasonography guidance is also available,[26] and vessel calcification can be a helpful landmark for selecting a puncture site.

A floppy, hydrophilic, or stiff wire can be engaged in the true lumen of the target vessel with the assistance of a low-profile support catheter or an over-the-wire balloon catheter, sometimes without sheath placement (Fig. 8B). Retrograde subintimal crossing can be implemented until entry into the proximal true lumen or the subintimal space from the antegrade approach is achieved. The technical success rate of the retrograde approach in previous studies was in the range of 85% to 86.3%.[26,27]

More recently, Palena and Manzi[28] reported the extreme application of the retrograde approach for transmetatarsal or transplantar arch access. In their 28 patients, transmetatarsal artery access was performed in 25 patients and transplantar access in 3 with a technical success rate of 86% and no major complications. This aggressive retrograde approach might serve as a last resort in patients with challenging CLI who are unsuitable for retrograde pedal or plantar access, although further investigation needs to be undertaken.

With respect to complications associated with the retrograde approach, pedal access site occlusion was observed in 1.9% of cases following unsuccessful procedures.[27] This complication can result in a catastrophic scenario on the verge of limb loss. In addition, the prognosis of CLI patients after retrograde access procedures remains unclear despite successful retrograde recanalization. There is a potential risk of puncture site occlusion during follow-up that can be repaired by angioplasty (Fig. 8C–E). Thus, prudent application of this technique is crucial.

Transcollateral Technique. Few reports regarding this technique are available. Fusaro et al.[29] first reported a challenging case using the transcollateral technique between the crural arteries. They successfully crossed an occlusion in the tibioperoneal trunk in a retrograde manner using a 0.014-inch hydrophilic guidewire through the developed collateral vessels of the anterior tibial artery into the peroneal artery. Leaving the first wire in place as a marker, the occlusion in the tibioperoneal trunk was crossed in an antegrade manner with another 0.014-inch wire and dilated with a balloon catheter. In the single-stage procedure, a long occlusion in the posterior tibial artery was also treated in a similar fashion using the collateral vessels from the peroneal artery to the posterior tibial artery. According to Montero-Baker et al.,[27] this transcollateral technique was undertaken in 11.8% of retrograde approaches after failed

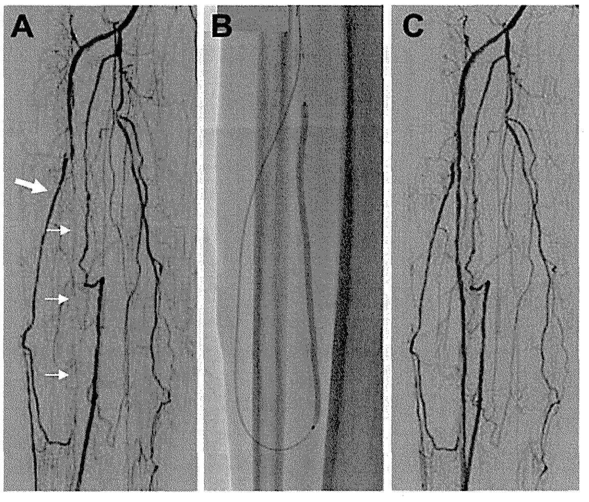


Figure 9 ◆ Transcollateral technique.(**A**) Baseline angiogram showing a CTO in the right anterior tibial artery (small arrows) with bridging collateral vessels (large arrow). (**B**) Retrograde crossing and angioplasty via the bridging collateral vessels. (**C**) Completion angiogram showing an excellent result after balloon angioplasty.

antegrade procedures. Bridging collaterals also can be used in this technique (Fig. 9A–C).

Transpedal Arch Technique (Transdorsal-to-Plantar or Transplantar-to-Dorsal). This technique can be indicated in peculiar cases requiring complete tibial revascularization. Even though no distal vessels for retrograde puncture are available in the setting of severe infrapopliteal artery disease, initial success in one antegrade tibial recanalization can provide an opportunity for using this technique to cross another tibial artery in a retrograde manner. Also, in the application of this technique, common variations in the anatomy of the arteries of the foot need to be taken into account. A successful procedure can provide better outflow for tibial arteries. However, procedure failure carries the potential risk of worsening foot ischemia.

In 2007, Fusaro et al.[30] initially described this technique using a 0.014-inch hydrophilic wire for the treatment of severe infrapopliteal disease, including tandem occlusions in the anterior tibial, dorsalis pedis, and posterior tibial arteries. In 2008, Kawarada et al.[21] reported complete revascularization of "serial" long total occlusions of the tibial arteries and the dorsalis pedis artery. They used this technique to cross an extensive CTO in the posterior tibial artery in a retrograde manner after successful subintimal angioplasty of an extensive CTO in the anterior tibial artery to the dorsalis pedis artery (Fig. 10A–D). Zhu et al.[31] reported the clinical application of trans-

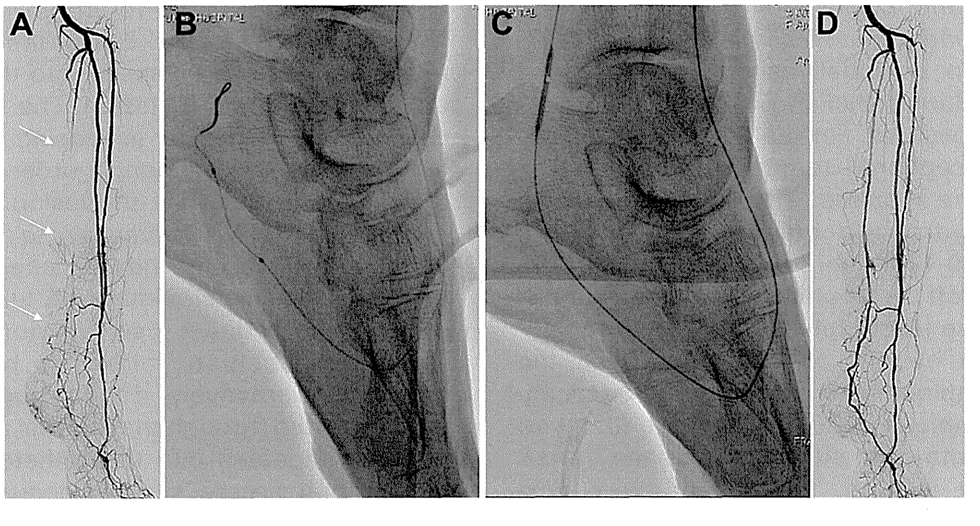


Figure 10 ◆ Transpedal arch technique. (**A**) Angiogram showing a lengthy CTO from the left posterior tibial artery to the plantar artery (arrows). (**B**) Retrograde access was attempted through the pedal arch after failed antegrade crossing. The J-loop technique with a 0.014-inch guidewire supported by an over-the-wire balloon catheter was used. (**C**) Successful crossing and balloon angioplasty. (**D**) Final angiogram showing complete revascularization. Reproduced with permission from Kawarada et al.[21] © Copyright 2008. John Wiley & Sons, Inc.

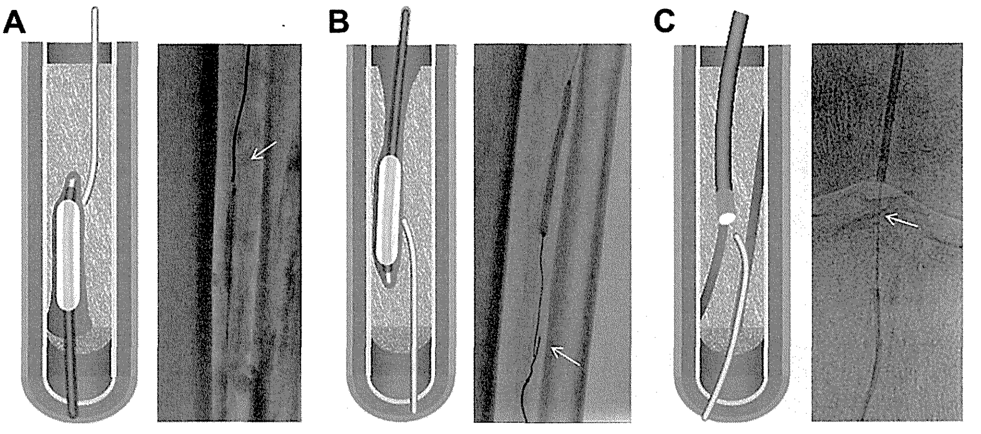


Figure 11 ◆ (**A**) CART technique: an antegrade guidewire (arrow) advances into the retrograde track. (**B**) Reverse CART technique: a retrograde guidewire (arrow) advances into the antegrade track. (**C**) Rendezvous technique: accommodating the retrograde guidewire (arrow) in the antegrade catheter. A color version is available online at *www.jevt.org*.

dorsal-to-plantar or transplantar-to-dorsal reentry following unsuccessful subintimal angioplasty for below-the-ankle occlusions. In their series, all the patients were diabetic and the technical success rate was 62.5% (5/8). According to Manzi et al.,[32] this technique was attempted in 10.1% (135 patients) of 1331 consecutive patients, with a success rate of 85%, limb salvage rate of 86%, and target vessel revascularization rate of ~8%.

Controlled Antegrade and Retrograde Tracking and Dissection (CART) / Reverse CART / Rendezvous Techniques. These techniques can potentially allow for successful crossing during challenging antegrade-retrograde procedures. For the guidewire manipulation, exceptional torque response and/or lubricity are required. Therefore, proper use of stiff hydrophilic guidewires [0.014-inch: Astato XS9-12 (Asahi Intecc); 0.018-inch: Astato] or soft hydrophilic guidewires [0.014-inch: Cruise (Asahi Intecc)] is indispensable.

Surmely et al.[33] originally described the CART technique as a coronary CTO recanalization technique in 2006. When the first wire strayed into the subintimal space in an antegrade fashion, the second wire was advanced via a "collateral vessel" in a retrograde fashion. In the setting of infrapopliteal CTO, the second wire is advanced through the "retrograde access." A balloon is advanced in a retrograde fashion and inflated in the CTO segment, enlarging the space to increase the likelihood of antegrade guidewire crossing (Fig. 11A).

Historically, the reverse CART technique was rarely used early in the development of retrograde coronary intervention, but it has sincebecome the most commonly used retrograde reentry technique in the field.[34,35] Currently, this technique is increasing in popularity in infrapopliteal CTO interventions (Fig. 11B). It involves placing a retrograde guidewire in the distal cap of the CTO and advancing another wire in an antegrade fashion in the proximal cap of the CTO. The retrograde wire is advanced into the subintimal space of the CTO lesion. The subintimal channel is enlarged by advancing and inflating an antegrade balloon in order to dissect the plaque and modify the lesion. Then the retrograde wire is advanced to cross the dissection and link up with the antegrade wire positioned in the proximal true lumen. Subsequent procedures can be done in the retrograde fashion following retrograde crossing. Alternatively, if the retrograde wire is externalized through the femoral access site or accommodated into the catheter through the femoral access site, subsequent procedures can be done in an antegrade fashion.

The rendezvous technique is also essential during challenging antegrade-retrograde procedures. This technique was originally reported by Kim et al.[36] for coronary CTO recanalization. They described a method in

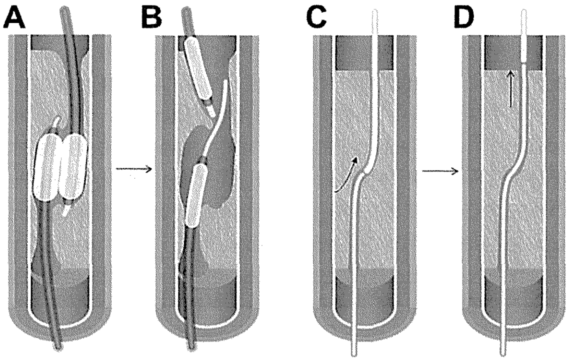


Figure 12 ◆ In the confluent balloon technique, (**A**) balloon catheters are simultaneously dilated to make a connection between the antegrade and retrograde lumens. (**B**) A retrograde guidewire is advanced into the antegrade path via the balloon catheter. For the kissing wire technique, (**C**) the guidewires are advanced from both directions. (**D**) A retrograde guidewire advances into the antegrade track of the guidewire. (An antegrade guidewire also advances into the retrograde track depending on circumstances.) A color version is available online at *www.jevt.org*.

which microcatheters are aligned in a guide catheter, followed by an antegrade guidewire being pulled into a retrograde microcatheter. Wu et al.[37] reported use of this technique as bailout in a patient in whom left main trunk dissection occurred during the CART technique. Current infrapopliteal CTO intervention can benefit from this technique. Retrograde guidewires can be advanced into the antegrade catheter at the rendezvous point (Fig. 11C). Shimada et al.[38] reported successfully combining the rendezvous technique and the transcollateral retrograde approach to recanalize a long total occlusion in the anterior tibial artery.

During these techniques, the confluent balloon technique may be necessary. In this method, simultaneous overlapping balloon dilation in the antegrade and retrograde subintimal space could lead to confluence of the subintimal space and subsequent successful guidewire passage through the newly created confluent subintimal space (Fig. 12A,B).[39] Without balloon dilation, this antegrade-retrograde technique can also be referred to as the kissing wire technique (Fig. 12C,D).[40]

Ankle Joint Movement during the Procedure. Infrapopliteal arteries are susceptible to multiple types of mechanical stress, such as flexion, torsion, expansion, and contraction due to ankle joint movement.[41] In the distal segment of the posterior tibial artery, plantarflexion can cause significant vessel kinks whereas dorsiflexion can straighten the kinks. In the dorsalis pedis artery, the opposite holds true: dorsiflexion can cause multiple kinks, whereas plantarflexion stretches them out. Furthermore, extensive plantarflexion can occlude the dorsalis pedis artery due to compression by the underlying bone (Fig. 13). Given these characteristics of the infrapopliteal arteries, appropriate flexion or extension of the ankle joint can straighten a bent

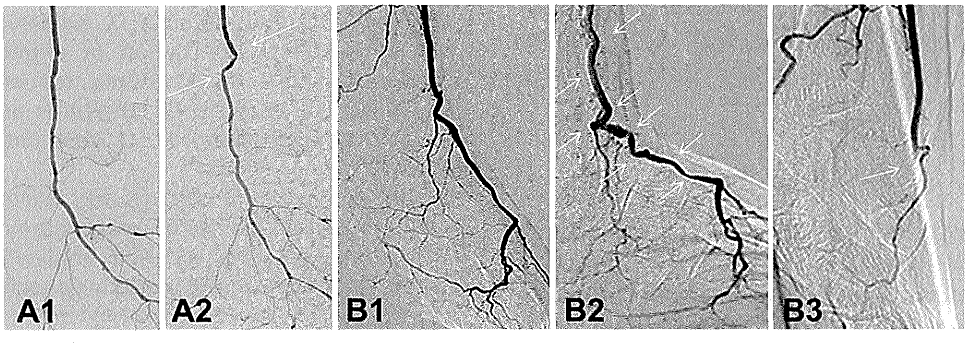


Figure 13 ◆ Extensive kinking related to ankle joint movement. (**A**) Distal posterior tibial artery and plantar artery (lateral image) in the (**A1**) normal position and (**A2**) plantarflexion, causing significant kinks (arrows). (**B**) Distal anterior tibial artery and dorsalis pedis artery (lateral image) in the (**B1**) normal position and (**B2**) dorsiflexion, causing multiple kinks (arrows). (**B3**) Plantar flexion causing occlusion of the dorsalis pedis artery due to compression by the underlying bone.

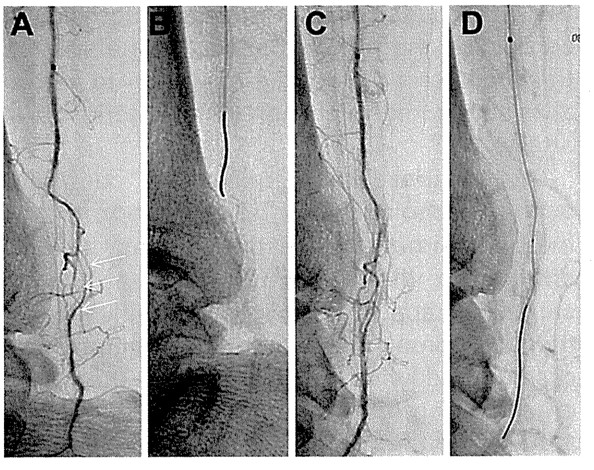


Figure 14 ◆ Ankle joint movement technique. (**A**) Occlusive lesion in the distal posterior tibial artery above the ankle joint (arrows). (**B**) Unsuccessful advancement of the guidewire. (**C**) Flexion of the ankle joint straightens the stenotic vessel, (**D**) facilitating successful lesion crossing.

distal occlusive segment to facilitate successful crossing (Fig. 14).

Application to Critical Hand Ischemia

Endovascular crossing techniques developed for infrapopliteal CTO intervention can be applied to the treatment of critical hand ischemia (CHI). Kawarada et al.[42] reported successful recanalization of an ulnar artery occlusion using a 0.014-inch CTO-dedicated guidewire. Gandini et al.[43] described "the radial to ulnar artery loop technique," which is similar to the transpedal arch technique. Thus, infrabrachial artery disease (below-the-elbow lesions) presenting with CHI can be treated using endovascular CTO crossing techniques.

CONCLUSION

This review presented a comprehensive summary of the practical application of contemporary infrapopliteal CTO crossing techniques. Patient-oriented strategies using these dedicated techniques can translate into further improvements in endovascular therapy. However, it is unclear as to whether and how these techniques can affect vessel patency and clinical outcomes such as wound healing and limb salvage. Since the case series described in this review might represent best case scenarios, success rates in real world practice may be lower and learning curves may be rather flat, but a combination of these techniques could increase the chance of successful crossing in challenging cases. We hope that principles described here will serve as a primer for infrapopliteal CTO intervention and a foundation for advancing the clinical study of infrapopliteal intervention.

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Variability in Quantitative and Qualitative Analysis of Intravascular Ultrasound and Frequency Domain Optical Coherence Tomography

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Background: Frequency-domain optical coherence tomography (FD-OCT) is an intravascular imaging technique now available in the United States. However, the importance of level of training required for analysis using intravascular ultrasound (IVUS) and FD-OCT is unclear. The aim of this study was to evaluate inter- and intra-observer variability between expert and beginner analysts interpreting IVUS and FD-OCT images. Methods and Results: Two independent expert analysts and two independent beginner analysts evaluated a total of 226 ± 2 stent cross-sections with IVUS and 232 ± 2 stent cross-sections with FD-OCT in 14 patients after stenting. Inter- and intra-observer variability for determining stent volume index (VI), as well as identifying incomplete stent apposition and dissection were assessed. The inter- and intra-observer variability of stent VI was minimal for both beginner and expert analysts regardless of imaging technology (random variability: 0.38 vs. 0.05 mm^3/mm for IVUS, 0.26 vs. 0.08 mm^3/mm for FD-OCT). Although qualitative IVUS analysis at the patient level revealed no significant difference between beginners and experts, this was not the case for FD-OCT. The number of overall qualitative findings noted by beginner and expert analysts were more variable (overestimated or underestimated) with FD-OCT. Conclusion: Despite varying levels of training, the increased resolution of FD-OCT compared to IVUS provides better detection and less variability in quantitative image analysis. On the contrary, this increased resolution not only increases the rate but also the variability of detection of qualitative image analysis, especially for beginner analysts.

Key words: inter-observer variability; intra-observer variability; optical coherence tomography; reproducibility; coronary imaging

INTRODUCTION

Accurate and reproducible assessment of intravascular imaging is critical for coronary catheterization procedure success, and may be dependent on both the imaging modality used and the level of training of the user. Intravascular Ultrasound (IVUS) is widely used as a diagnostic modality complementary to coronary angiography and has been the reference standard for understanding atherosclerosis [1]. Frequency-domain optical coherence tomography (FD-OCT), which recently became commercially available in the United States, is based on near-infrared light reflectivity [2,3]. It produces a higher resolution image (10–15 μm) as compared to IVUS (150–200 μm), possibly enabling more accurate and reproducible evaluation, although the importance of experience in assessing these images has not been assessed [4–6]. To our knowledge, there are no published data with respect to the importance of experience in interpreting IVUS versus FD-OCT images. Therefore, the aim of this study is to explore how the imaging modality and the level of training of the analyst affects the accuracy and/or reproducibility

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of quantitative, as well as qualitative evaluation of IVUS and FD-OCT images after stent implantation.

METHODS

Patients

Patients who met the following inclusion and exclusion criteria were enrolled in this study. Major inclusion criteria were (1) single de novo coronary artery lesion treated with currently approved drug-eluting stents, (2) lesions treated with a single stent, (3) lesion length less than 24 mm, and (4) reference diameter between 2.0 and 3.5 mm. Major exclusion criteria were (1) acute myocardial infarction and (2) left main and/or ostial lesion.

The protocol was approved by the Stanford University Institutional Review Board, and all patients gave written informed consent before the procedure.

IVUS and FD-OCT Procedure

The IVUS procedure was performed in standard fashion using automated motorized pullback (0.5 mm/sec) with a commercially available imaging system (40-MHz catheter, Boston Scientific Corp, Natick, MA, or 45-MHz catheter, Volcano, Rancho Cordova, CA). The FD-OCT images were obtained with an FD-OCT system (C7-XR system, LightLab Imaging, Inc., Westford, MA, now St. Jude Medical, St. Paul, MN) with undiluted contrast media continuously flushed through the 6Fr guiding catheter without side holes by a power injector (4 ml/sec, 3.5 sec duration). During the flushing process, motorized pullback FD-OCT imaging was performed at a rate of 20 mm/sec for a length of 50 mm.

IVUS and FD-OCT Analysis

Volumetric measurements were performed using PC-based software (echoPlaque version 3.060, Indec Systems Inc, Santa Clara, CA). Stent volume index (VI, mm^3/mm) was calculated by dividing the stent volume by the stent length measurement. Incomplete stent apposition (ISA) and dissection were assessed using qualitative analysis. On the basis of the IVUS images, ISA was defined as one or more struts clearly separated from the vessel wall with evidence of blood speckles behind the strut [7]. On the basis of the FD-OCT images, ISA was defined as separation of a stent strut from the inner vessel wall by a distance greater than the nominal strut plus polymer thickness [8]. For both imaging modalities, dissection was defined as a disruption of the vessel luminal surface, including flaps or cavities [9]. On the basis of the FD-OCT images, intra-stent dissection was defined as a disruption of the vessel luminal surface in the stent segment. Note that because intra-stent dissection cannot be reliably differentiated from plaque prolapse with IVUS because of limitations of axial resolution [9], this evaluation was not included in IVUS versus FD-OCT comparisons.

IVUS and FD-OCT images were analyzed by two independent expert analysts and two independent beginner analysts. The measurements within either expert or beginner groups were compared to determine the inter-observer variability. Blind analyses were repeated by the same observer after an interval of at least 4 weeks and these measurements were compared to determine intra-observer variability. Expert analysts were those who had worked for at least 2 years as intravascular imaging researchers and, as such, had extensive experience interpreting both IVUS and FD-OCT images. These individuals were certified by the Cardiovascular Core Laboratory at Stanford University. The beginner analysts were physicians with no prior hands-on experience interpreting IVUS or FD-OCT images and underwent a 2 hour training session by experts in the Cardiovascular Core Laboratory at Stanford University upon joining the study. In addition, a consensus panel of three independent experts at Stanford University's Cardiovascular Core Laboratory reviewed all cases and served as the gold standard.

Statistical Analysis

Statistical analysis was performed with SPSS version 18.0 (SPSS, Chicago, IL). Categorical variables were presented as counts and percentages. Continuous variables were presented as mean values ± standard deviation (SD). Comparison of each parameter was made using linear regression and the Bland–Altman test [10]. The inter- and intra-observer agreement (reproducibility) was assessed by determining the mean and SD of the between-observation and between-observer differences, respectively. In addition, qualitative analysis was compared to the gold standard. A P value of <0.05 indicated statistical significance.

RESULTS

Baseline Characteristics

The baseline demographics of 14 patients who underwent percutaneous coronary intervention of a single lesion followed by both IVUS and FD-OCT imaging are summarized in Table I. On average, 226 ± 2 stent cross sections per patient were evaluated with IVUS and 232 ± 2 with FD-OCT. The minor difference in the number of stent cross sections evaluated by the two technologies was because of their different image acquisition rates.

TABLE I. Baseline Characteristics

	$N = 14$
Number of evaluated stent cross sections	233
Age (yr)	68 ± 9
Male gender, % (*n*)	86% (12)
Target lesion (%) LAD/LCX/RCA	21/43/36
Coronary risk factors, % (*n*)	86% (12)
Hypertension	100% (14)
Hyperlipidemia	36% (5)
Diabetes	
Prior myocardial infarction (%)	36% (5)
Prior percutaneous coronary intervention (%)	50% (7)
Frequency of pre-dilatation (%)	79% (11)
Frequency of post-dilatation (%)	100% (14)
Type of stent (%) Cypher/Taxus/Xience V/Endeavor	14 / 7 / 64 / 14
Average stent diameter (mm)	2.7 ± 0.2
Average stent length (mm)	15.3 ± 4.1

LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Quantitative Analysis

There was a good correlation between beginner and expert analysts ($R = 0.945$–0.991) and between expert and expert analysts ($R = 0.996$) for measuring stent VI based on IVUS images. Bland–Altman testing showed minimal inter-observer variability for both beginner and expert analysts (random variability 0.38 vs. 0.05 mm^3/mm) (Fig. 1A).

There was good correlation between beginner and expert analysts ($R = 0.991$–0.999) and between expert and expert analysts ($R = 0.998$) for measuring stent VI based on FD-OCT images. Bland–Altman testing showed similar random inter-observer variability for both beginner and expert analysts (0.26 vs. 0.08 mm^3/mm) (Fig. 1B).

The intra-observer variability of stent VI was minimal for both beginner and expert analysts regardless of imaging technology (random variability: 0.16 and 0.06 mm^3/mm for beginner, 0.03 and 0.04 mm^3/mm for expert) (Fig. 2).

Qualitative Analysis

Significantly more examples of ISA and edge dissection were identified on FD-OCT image analysis as compared to IVUS image analysis by both beginner and expert analysts (Table III). The detection of ISA and edge dissection at the patient level based on evaluation of IVUS images showed lower inter-observer agreement among beginner as compared to expert analysts, but these differences did not reach statistical significance (64% for beginners and 79% for experts, $P = 0.678$, Table II). The detection of edge dissection and intra-stent dissection based on evaluation of FD-OCT images revealed significantly higher inter-observer agreement among the experts compared with the beginners (50% for beginners and 93% for experts with respect to edge dissection, $P = 0.033$, and 0% for beginners and 36% for experts with respect to intra-stent dissection, $P = 0.041$, Table II). Although there was also a trend toward higher inter-observer agreement among the experts compared with the beginners for detecting ISA with FD-OCT, this was not statistically significant (36% for beginners and 71% for experts, $P = 0.058$, Table II). Beginner analysts showed significantly greater intra-observer variability compared with expert analysts with both IVUS (64% for beginners and 100% for experts with respect to ISA, $P = 0.041$) and FD-OCT image analysis (14% for beginners and 93% for experts with respect to intra-stent dissection, $P \leq 0.001$), except for the identification of edge dissection (Table II).

The total number of each finding is shown in Table III. In terms of the overall number of findings noted by beginner and expert analysts, they were similar with IVUS analysis, and more variable with FD-OCT. The IVUS image evaluation inter-observer agreement between either beginner or expert analysts and our gold standard analyst group was not statistically different for the detection of either ISA or edge dissection (Table IV), although there was a trend toward overestimation of findings among beginners, especially in the detection of ISA (Table III). In terms of FD-OCT image analysis, inter-observer agreement between either beginner or expert analysts and our gold standard analyst group was not significantly different, except for the detection of edge dissection, which was poorer among beginners (Table IV). Similarly, beginners had a higher variability in both over- and underestimation of FD-OCT findings compared with expert analysts, except for intra-stent dissection (Table III). Figure 3 demonstrates examples of differences in interpretation between beginners and experts with regard to side branch structures versus dissection. There were no significant differences for intra-observer agreement for beginners or experts at the lesion level for IVUS or FD-OCT (Table IV).

DISCUSSION

Our main findings in this study comparing the ability of beginner and expert analysts to interpret IVUS and FD-OCT images are as follows: (1) There was less inter-observer and intra-observer variability of the quantitative analyses by both beginners and experts with FD-OCT image analysis as compared to IVUS; (2) The number of overall qualitative findings were significantly greater and more variable amongst the