JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 4, NO. 9, 2011

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
DOI: 10.1016/j.jcin.2011.06.011

STATE-OF-THE-ART PAPER

Fundamental Wire Technique and Current Standard Strategy of Percutaneous Intervention for Chronic Total Occlusion With Histopathological Insights

Satoru Sumitsuji, MD,* Katsumi Inoue, MD,† Masahiko Ochiai, MD,‡
Etsuo Tsuchikane, MD,§ Fumiaki Ikeno, MD||

Osaka, Kitakyushu, Yokohama, and Toyohashi, Japan; and Palo Alto, California

Currently, successful treatment of chronic total occlusion (CTO) seems markedly improved, due to several new techniques and dedicated device developments. However, this improved success rate is often limited to procedures performed by skilled, highly experienced operators. To improve the overall success rate of percutaneous coronary intervention of CTO from a worldwide perspective, a deeper understanding of CTO histopathology might offer insights into the development of new techniques and procedural strategies. In this review, CTO histopathology and wire techniques are discussed on the basis of the fundamental concepts of antegrade and retrograde approaches. Although details pertaining to wire manipulation are very difficult to explain objectively, we tried to describe this as best as possible in this article. Finally, a systematic review of the current standard CTO strategy is provided. Hopefully, this article will enhance the understanding of this complex procedure and, consequently, promote safe and effective CTO-percutaneous coronary intervention for patients who present with this challenging lesion subset.
(J Am Coll Cardiol Intv 2011;4:941–51) © 2011 by the American College of Cardiology Foundation

Chronic total occlusion (CTO) remains a challenging lesion subset in percutaneous coronary intervention (PCI), because of lower initial success rates (1,2) and higher rates of restenosis in the chronic phase (1). Currently, the introduction of drug-eluting stents has resulted in improved patency of CTO in the chronic phase (3), and due to several new techniques and dedicated device developments, the initial success of opening CTO seems to be markedly improving as well (4–7). Yet these improved success rates are often limited to patients whose procedures were performed by highly skilled, experienced operators. We investigated the techniques of skilled CTO interventional operators and their strategies with an emphasis on 4 insights unique to CTO-PCI: 1) understanding the histopathology of CTO; 2) wire techniques with understanding of the histopathology of CTO; 3) fundamentals of wire manipulation; and 4) systematic review of current CTO-PCI strategy. Thus, the purpose of this article is to offer these 4 insights of CTO-PCI, which hopefully will result in higher initial success of CTO-PCI for more patients presenting with this challenging lesion subset.

Histopathology of CTO

An improved understanding of CTO histopathology is important not only to help to improve success rate but also to develop new techniques and

From the *Nozaki Tokushukai Hospital, Nagoya Tokushukai General Hospital and Osaka University, Osaka, Japan; †Kokura Memorial Hospital, Kitakyushu, Japan; ‡Showa University, Northern Yokohama Hospital, Yokohama, Japan; §Toyohashi Heart Center, Toyohashi, Japan; and the ||Stanford University, Palo Alto, California. Dr. Sumitsuji has served on the Speakers' Bureau for Abbott Vascular, Asahi Intec, Biosensors, Johnson & Johnson (Cordis), and Terumo; and as consultant to Goodman and Zio Software. Dr. Ochiai has served on the Speakers' Bureau for Abbott Vascular, Asahi Intecc, Boston Scientific, and Terumo. Dr. Tsuchikane has served on the Speakers' Bureau for Asahi Intecc, Abbott Vascular, Boston Scientific, and Johnson & Johnson (Cordis). Dr. Ikeno has served as consultant to Asahi Intecc and Terumo. Dr. Inoue has reported that he has no relationships relevant to the contents of this paper to disclose.

Manuscript received November 30, 2010; revised manuscript received June 15, 2011, accepted June 23, 2011.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:941–51

strategies for CTO-PCI. Herein, 3 important histopathological topics are presented.

Histopathological process of CTO progression. The histopathological process of CTO progression is not clearly understood. One widely held belief is that, once the coronary artery occlusion occurs, thrombus formation develops up to the side branch ostium (8,9). These thrombi then change into organized thrombus that is more rigid than fresh thrombus formation, with a dense concentration of collagen-rich fibrous tissue at the proximal and distal ends of the lesions, referred to as proximal and distal fibrous caps, respectively (9) (Fig. 1). In the autopsy analysis of this study, the intimal plaque of shorter-duration CTO was highly fibrotic plaque with calcified lesions, whereas the original lumen area mainly consisted of organized thrombus with microchannels defined as small lumen in CTO lesion with an average size of 200 μm (8,9) (Fig. 2A). In contrast, longer-duration CTO contained harder intimal plaque and more dense calcium formations without microchannels (Fig. 2B), supporting findings of previous reports (8,9).

Abbreviations and Acronyms

Ante = antegrade approach

CART = controlled antegrade and retrograde tracking

CT = computed tomography

CTO = chronic total occlusion

IVUS = intravascular ultrasound

PCI = percutaneous coronary intervention

Retro = retrograde approach

STAR = subintimal tracking and re-entry

Microchannel, loose tissue segments. In theory, the success of wire crossing in CTO-PCI might be affected by loose fibrous tissue, pultaceous debris, or intra-intimal plaque microchannels (8,10). In limited reports, most of the microchannels in CTO lesions lead into the adventitia and are likely to be located in the intimal side (8,9). In an autopsy analysis, Katsuragawa et al. (11) reported that the microchannels often extend to the small side branches and vaso vasorum, whereas others continue longitudinally from the proximal lumen to the distal lumen.

There are considerable animal model data about microchannels in CTO. In an experimental rabbit femoral artery CTO model, microcomputed tomography demonstrated that extravascular microchannels are seen mostly in the early phase of artery occlusion, and in more mature CTO, intravascular microchannels increase gradually (12). Yet once the CTO has matured, the number of both extra- and intravascular microchannels become much fewer, compared with the early phase (12). Upon further analysis, the longitudinal continuity of microchannels extended to approximately 85% of the entire CTO length, except in the early phase of CTO (12).

In reports of loose tissue segments in CTO, Katsuragawa et al. (11) reported that continuous loose tissue is frequently seen in the tapered entry type of CTO as well as in the short-occlusive-length CTO. Of interest, 4 of 10 autopsy CTO specimens in the Katsuragawa et al. (11) report and 78% of the Srivatsa autopsy CTO specimens were found not to be totally occluded upon pathological examination, despite angiographic evidence of total occlusion (8,11). Moreover, in all 4 cases of the Katsuragawa et al. (11) report, the loose tissue was located continuously from the proximal to the distal end (11), whereas Srivatsa et al. (8) concluded that the thrombus inside the microchannels might have "melted" during specimen fixation. In view of these data, histopathological non-occluded lesions probably consist of loose tissue with microchannels. Furthermore, Srivatsa et al. (8) reported that the existence of a non-occluded lesion did not relate to CTO age, suggesting that loose tissue exists, even in old CTOs, offering an explanation for successful loose tissue tracking, even in old CTOs.

Intimal/subintimal space. Both "intima" and "subintima" are key aspects of pathological information in CTO-PCI. Figure 3 shows images from a pathology examination of the coronary artery from a patient who died due to retroperitoneal hemorrhage after unsuccessful CTO-PCI complicated by a large dissection. All slices show the large dissection with hematoma in the subintimal space. This dissection is located between the intima and adventitia, in the so-called media, especially near the external elastic lamina. This area

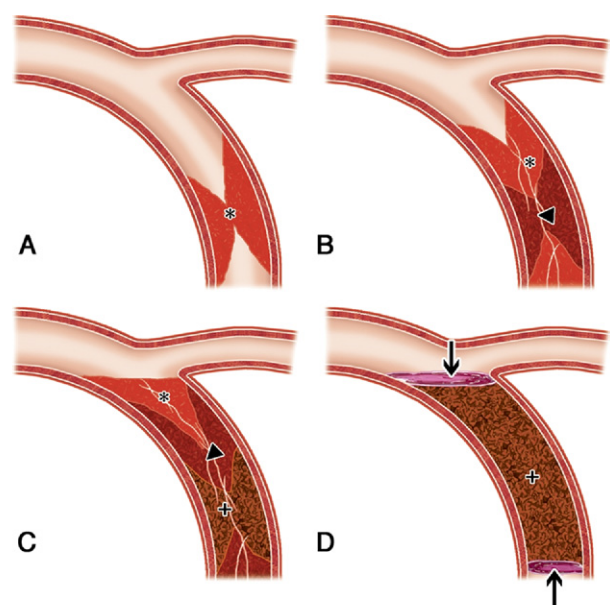

Figure 1. Progression of Chronic Total Occlusion: Extending and Organizing Thrombus

(A) The obstruction of coronary artery with fresh thrombus. Fresh thrombus **(*)**. **(B)** Thrombus formation develops proximally **(*)** and distally. The original thrombus turns into organized thrombus **(arrowhead)**. **(C)** Thrombus formation develops up to the side branch ostium. The originally occluded area turns into fibrotic plaque with calcified lesions **(+)**. **(D)** Aged chronic total occlusion with fibrotic plaque and calcified lesions **(+)**. Each **arrow** indicates proximal and distal fibrous cap.

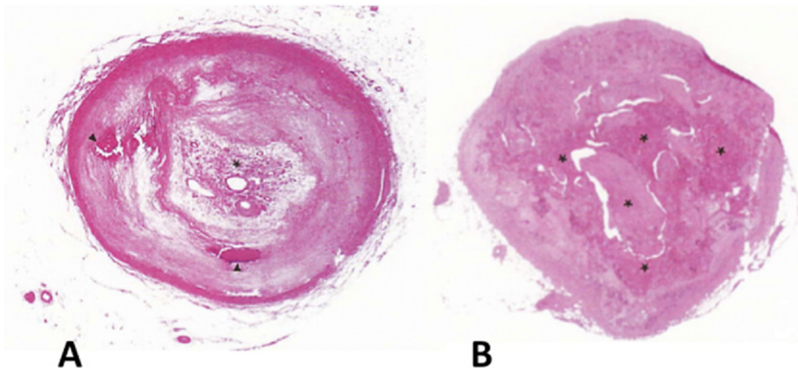

Figure 2. Histopathological Images of Chronic Total Occlusion

The cross-sectional histopathological images of angiographically occluded coronary artery in the different occluded period. **(A)** 1.5-year chronic total occlusion that has organized thrombus with microchannel in original lumen area **(*)** with some calcification **(arrowhead)** in dense fibrous tissue. **(B)** 5-year chronic total occlusion in which much calcium **(*)** was observed without microchannels.

consists of histologically weak connected tissue; thus the dissection expands easily and widely in both longitudinal and transverse directions (Fig. 3D). This subintimal space is thought to be the same as the intramural hematoma in intravascular ultrasound (IVUS) examination (Fig. 4).

Wire Techniques With Understanding of CTO Histopathology

With this information of CTO pathology as a backdrop, wire techniques for CTO-PCI will be discussed. The fundamental

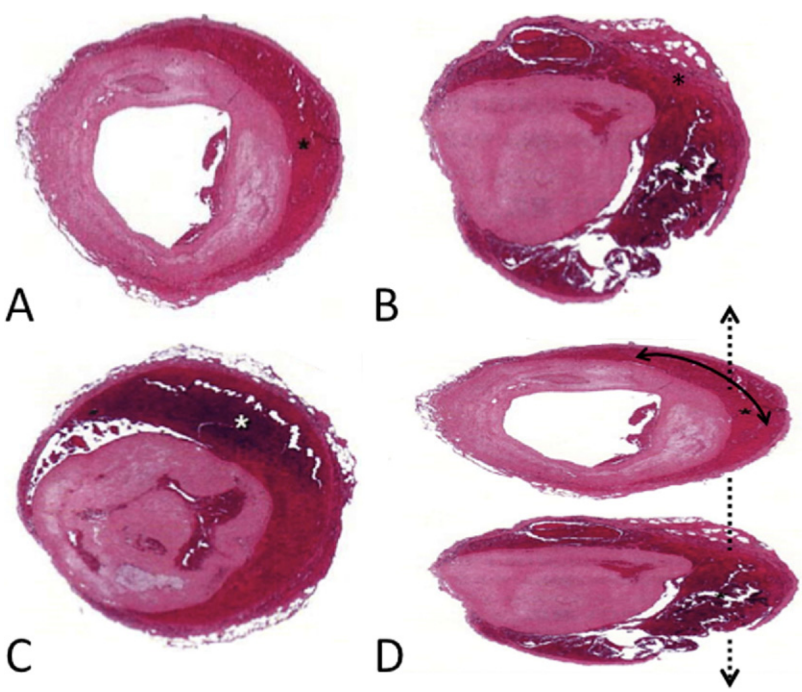

Figure 3. Histopathological Subintimal Space After Chronic Total Occlusion Procedure

Histopathological subintimal space **(*)**. **(A)** Proximal true lumen site; **(B)** chronic total occlusion site; **(C)** distal true lumen site; true lumen was collapsed by extended subintimal space; **(D)** subintimal space extension, transversely **(solid arrow)** and longitudinally **(dotted arrow)**.

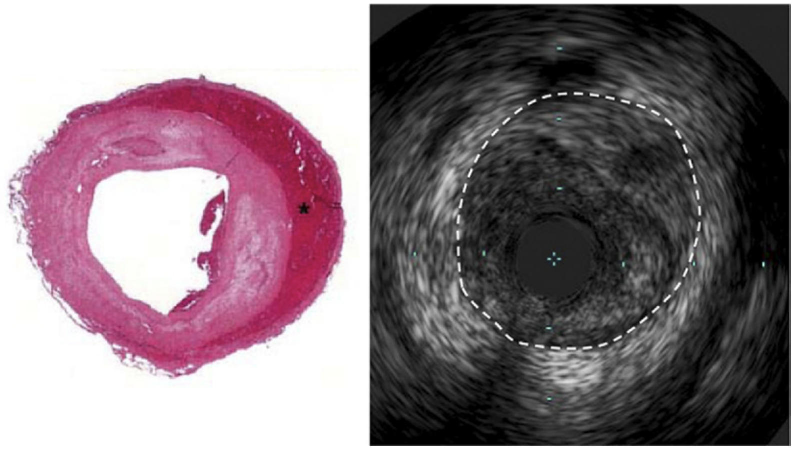

Figure 4. Comparison of Histopathological Subintimal Space and IVUS Interpretation as Intramural Hematoma

Intravascular ultrasound (IVUS) images taken during the procedure of chronic total occlusion percutaneous coronary intervention. Although these 2 images are from different patients, a good comparison is observed between the histopathological subintimal space **(*)** and IVUS intramural hematoma images. The IVUS image shows the higher echoic area outside of the intimal plaque, which corresponds to the dissection part in the pathological image. This IVUS image area indicates intramural hematoma. **Dotted circle** indicates external elastic lamina border.

concepts for the antegrade approach (Ante) and the retrograde approach (Retro) will be discussed separately.

Antegrade wire procedure. In the antegrade wire procedure, plaque tracking should be described as either intimal or subintimal. In addition, antegrade intimal plaque tracking has 2 techniques: loose tissue tracking and intentional intimal plaque tracking.

Antegrade loose tissue tracking. According to the information gleaned from both histopathological examinations and animal CTO model research, angiographically occluded lesions might possibly contain loose tissue segments in both short-duration CTO as well as old CTO (8,11). Matsukage et al. (13) reported that an intermediate-stiffness, 0.010-inch wire successfully crossed approximately 70% of CTO cases in the PIKACHU (Prospective Multicenter Registry of IKAzuchi-X for CHronic Total OcclUsion) trial; hence, these results might support the existence of loose tissue segments inside CTO. If the wire tip can be controlled and directed so that it will not penetrate hard atherosclerotic plaque, the wire will automatically advance with tracking in the loose tissue segments (Fig. 5). This is the concept of loose tissue tracking. However, it is not clear which tip-strength wire should be selected for this loose tissue tracking, because each case has a different degree of tissue rigidity. In the PIKACHU trial, loose tissue tracking was performed with only a 1.0-g tip-strength hydrocoated wire (13). Although it is a reasonable strategy not to use a stiff wire that could potentially penetrate the plaque easily as a primary wire, aspects of wire handling and movement in loose tissue tracking are similar to those of acute myocardial infarction cases, in that the wire is advanced easily and smoothly, only with multiple rotations of the wire tip (Online Video 1).

Antegrade intentional intimal plaque tracking. When it is impossible to cross the wire with loose tissue tracking, the wire should then be manipulated into the intimal plaque

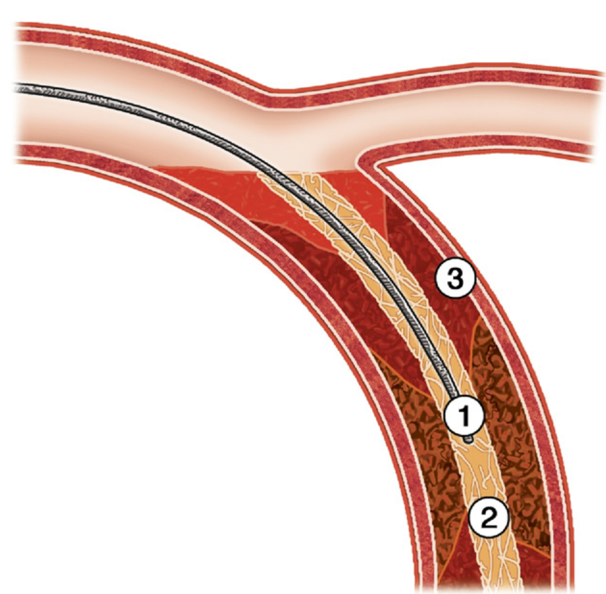

Figure 5. Principle of "Loose Tissue Tracking"

① indicates wire-tip force, ② indicates resistance in loose tissue, and ③ indicates resistance in plaque. If we can control ①, between ② and ③, like ② < ① < ③, wire might easily pass the chronic total occlusion (Online Video 1).

intentionally; thus we have named this technique "intentional intimal plaque tracking." Compared with subintimal tracking (as explained in the next section), intimal plaque tracking yields higher success rates of entering the true lumen at the distal vessel; so this procedure should be selected before performing subintimal tracking. This might be because the relative resistance in penetrating the true lumen is different between cases of the wire tip being located in the intimal plaque and cases of the wire tip being located in the subintimal tissue. The resistance of subintimal tissue against the wire tip is much lower than that toward the true lumen, so the wire seems to easily remain in the subintimal layer, making it hard to redirect the wire tip toward the true lumen (Fig. 6), resulting in failure to enter the distal true lumen. By contrast, 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 sometimes disturbs the wire crossing to the true lumen, which results in procedural failure. The crux of intentional intimal plaque tracking is to handle the wire intentionally by understanding where the wire tip is and in which direction the wire should be advanced. Images and data from IVUS, computed tomography (CT), and angiography are useful adjuncts for an enhanced understanding of these aspects (14). Of these, CT provides 3-dimensional information of the CTO, along with the diameter of the occluded vessel and calcification inside the CTO (14) to better enable precise antegrade intentional intimal plaque tracking.

When the side branch is located at the entrance of the CTO, the IVUS catheter can be inserted into the side branch to examine the place of wire penetration (15) (Fig. 7). Furthermore, if the IVUS catheter can possibly be inserted into the subintimal space, the operator can evaluate the direction of the intimal plaque and true lumen (16). However, insertion of the IVUS catheter into the subintimal space has the potential risk of enlarging the subintimal space; as a result, the true lumen might be collapsed by the compression of this subintimal space, causing the failure of the wire to cross. Although it is difficult to appreciate wire position with angiographic information, the "Sigmoid Curve Sign" is useful to detect subintimal tracking (Figs. 6 and 8). If the wire is running in a sigmoid shaped curve with the same width as the vessel diameter, subintimal tracking should be suspected. In this situation, CT information about vessel occlusion, diameter, and tortuosity helps to better understand this. Even when the CTO-dedicated wire is used, the intentional intimal plaque tracking is sometimes difficult to achieve because of calcified lesions in the CTO segment or severe tortuosity, thereby resulting in subintimal wire migration.

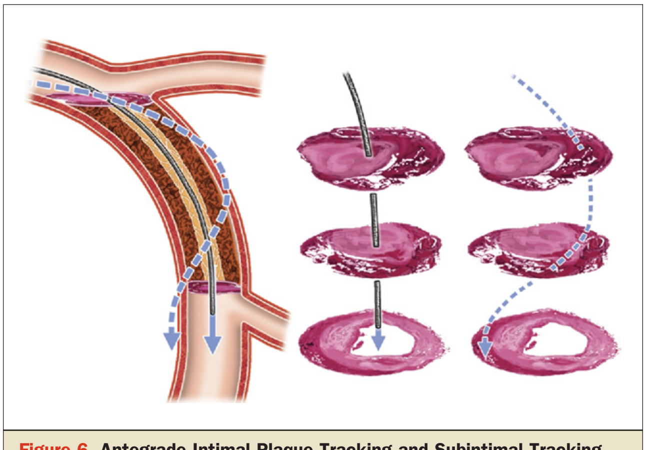

Figure 6. Antegrade Intimal Plaque Tracking and Subintimal Tracking

Antegrade intimal plaque tracking **(solid line)** and subintimal tracking **(dotted line)**. Once the wire migrated into the subintimal space, the wire easily advances into the subintimal space yet is difficult to cross to the distal true lumen because of lower resistance to advance into subintimal space coupled with increased resistance to traversing the plaque.

Antegrade subintimal tracking. Once the wire advances into the subintimal tissue, it is difficult to enter the true lumen without dedicated re-entry techniques and/or technologies, because intimal plaque located between the true lumen and subintima is more resistant than the subintimal tissue. This is especially true if the subintimal tissue is weak longitudinally, where the wire will tend to advance longitudinally without penetrating toward the true lumen (Fig. 6). Furthermore, enlargement of the subintimal space pushes the plaque toward the distal true lumen, resulting in its collapse. Both of these situations make wire crossing more difficult and increase the risk of ischemic myocardial injury. However, it is common for the wire to go into the subintimal space due to vessel tortuosity and calcified lesions. There are some methods to manage antegrade subintimal tracking. The re-entry technique with stiff wire requires that the wire-tip strength be directed from the subintima toward the true lumen as well as having the strength to penetrate the tissue located between true lumen and subintima. Although not easy to perform, selecting the re-entry position in the bending part or the bifurcated part of the vessel affords a greater chance at succeeding in re-entry. The subintimal tracking and re-entry technique (STAR) technique has been reported previously as an option of re-entry technique (17). The re-entry in the STAR technique occurs at the distal larger side branch bifurcation, because the strong wire tip can be easily directed from the subintima toward the true lumen. Although previous reports cite that cardiac function after the STAR technique is maintained, it should be noted that this technique has the potential risk of incomplete revascularization due to side branch occlusion. New techniques and systems, such as "contrast STAR," "Limited Subtintimal Tracking and Reentry technique," and "Bridgepoint Re-Entry System" might contribute to the success of re-entry (18,19); however, it still poses the risk of side branch occlusion(s). These new

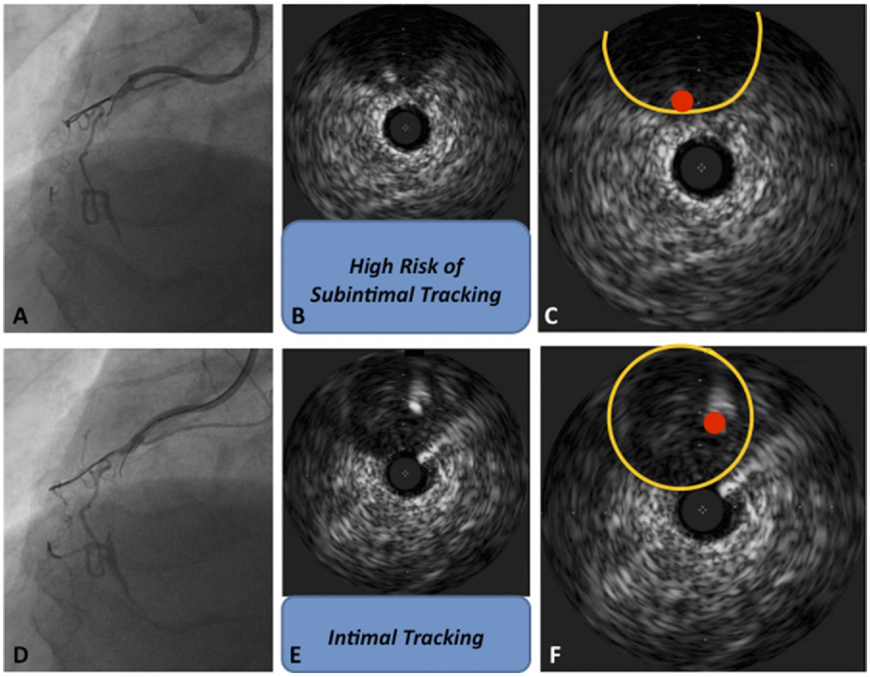

Figure 7. Intravascular Ultrasound Images of the Entry Point in Proximal-Mid Right Coronary Artery Chronic Total Occlusion

In this case, the uncertain residual channel was first pointed out at the chronic total occlusion entry, and then the wire was advanced into this uncertain channel. However, intravascular ultrasound information taken with intravascular ultrasound catheter advanced into the proximal right ventricular branch showed the wire was located close to the external elastic lamina **(A, B, C)**, and the wire was at great risk of migrating into the subintima. The stiff wire was advanced toward the more inner aspect of the vessel at the chronic total occlusion entry, and then the wire position was changed into the intimal plaque **(D, E, F)**. Finally, this wire successfully crossed the chronic total occlusion. **Red dot** indicates the wire. **Yellow circle** indicates the vessel border.

techniques and systems are reserved as the last resort for CTO-PCI recanalization.

Retrograde wire procedure. The fundamental theory of the Retro is quite different from the Ante. In the Retro, subintimal tracking is considered a factor of success rather than failure; thus, it is not necessary to avoid subintimal tracking in the Retro. Discussions regarding the Retro in intimal plaque tracking and subintimal tracking follow.

Retrograde intimal plaque tracking. In the Retro, subintimal tracking is important (20); however, IVUS examination after retrograde CTO-PCI revealed that 60% of cases were actually intimal plaque tracking (21). In retrograde intimal plaque tracking, 1 important aspect of CTO histopathology to keep in mind is that the distal fibrous cap is less rigid compared with that of the proximal fibrous cap (9). The proximal fibrous cap, which is the entry point of CTO for

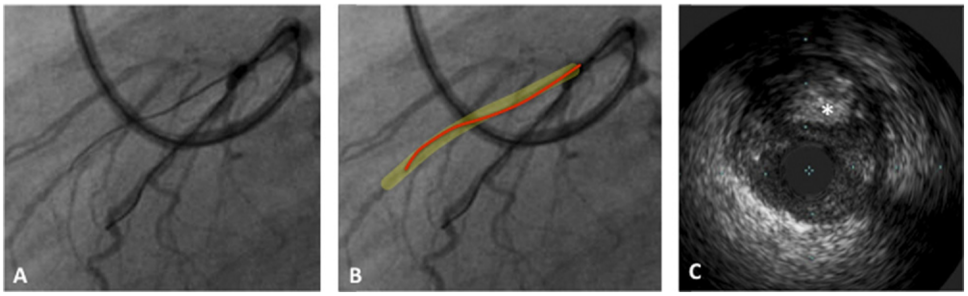

Figure 8. Representative Case of Subintimal Tracking

(A, B) The wire was formed into a large sigmoid shape inside a chronic total occlusion, and the wire tip migrated into the false lumen with angiographic information. In this situation, subintimal tracking was suspected from the sigmoid shape curve being the same width as the vessel diameter. **(C)** Subintimal tracking was confirmed by intravascular ultrasound during the procedure. The intravascular ultrasound catheter is located in the subintimal lumen. Intimal plaque **(*)**.

the Ante, is at higher risk of wire migration into the subintimal space, whereas the distal fibrous cap, which is the entry point of CTO for the Retro, is at lower risk of subintimal migration due to its weakness. When intimal plaque tracking is suspected by the wire position, it is worthwhile to control the wire carefully to enter the proximal true lumen directly. Although the operator is not mandated to use intimal plaque tracking in the Retro, perforation should be noted as a potential risk, especially when using a stiff wire, because the retrograde wire is traveling through the tortuous long collateral channel—so, at times, wire manipulation is restricted, even when using a microcatheter, which requires greater attention.

Retrograde subintimal tracking. Subintimal tracking is the key to success when using the Retro approach (20). Figure 9 demonstrates why subintimal tracking is not an issue in retrograde wiring. When the antegrade wire is advanced into the subintimal space, it enables placement of both antegrade and retrograde wires into the same space if the retrograde wire is advanced into the subintimal space. As mentioned previously, this can be achieved due to the nature of the subintimal space being easily dissected both transversely and longitudinally. Figure 10 depicts a representative case of retrograde subintimal tracking, where it is important to dilate the subintimal space enough to advance both the antegrade and retrograde wires into the same space. In this procedure, IVUS information is useful to determine the proper balloon size to dilate the subintimal space. In retrograde subintimal tracking, it should be noted that contrast injection should be avoided if at all possible, because this might enlarge the subintimal space and cause distal dissection. Enlargement of the subintimal space might result in the need for additional stent deployment, and in the worst case, failure of recanalization might result. To avoid these potential procedural issues, the authors recommend performing IVUS interrogation and balloon dilation before contrast injection.

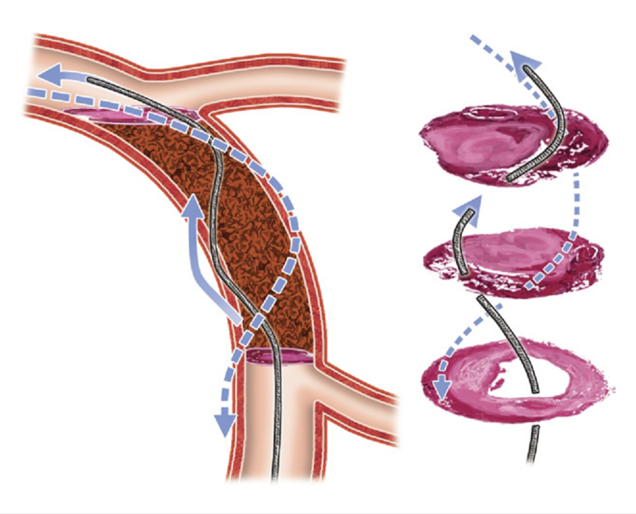

Figure 9. Principle of Retrograde Subintimal Tracking

Antegrade subintimal tracking **(dotted line)** and retrograde subintimal tracking **(solid line)**. Even though the angiogram shows that the 2 wires are separated (antegrade and retrograde), both wires can be positioned in the same subintimal space. After the retrograde wire comes into the same lumen with the antegrade wire, crossing into the proximal true lumen with the retrograde wire is highly promising.

Fundamentals of Wire Manipulation

Wire manipulation is of utmost importance for the initial success of CTO-PCI. However, it is challenging to accurately explain wire manipulation objectively, thus making CTO-PCI techniques more difficult to comprehend. After the introduction of the Retro, the contribution of this ingenious wire manipulation becomes less important to achieve successful wire crossing. However, careful wire manipulation is critically essential for antegrade intentional intimal plaque tracking. As mentioned previously, though tactile sensations stemming from the wire tip are difficult to explain with an objective description, we have attempted to describe this in order for other PCI operators to achieve higher success rates for their CTO-PCI cases.

The shape of the wire tip in CTO-PCI. Currently, the standardized consensus of the wire-tip curve has not yet been established. However, 1 of the common techniques of shaping the wire tip in Japanese CTO operators is shown in Figure 11 and Online Video 2. The important key point is to make a small curve of the wire tip with a 40° to 60° bend at 1 to 2 mm from the tip. And sometimes, the additional shallow second bend is made at 10 to 15 mm from the tip. The common way to make the bend is that the wire tip coming out of the wire-introducer is pressed gently with the finger to make the curve (Online Video 2).

Fundamental technical tips of wire manipulation in CTO-PCI. Basically, there are 2 different types of wire manipulation. One is the "both hands maneuver," and the other is the "right hand maneuver." In the "both hands maneuver," the left hand is used for to-and-fro movement and the right hand is used for rotation (Online Video 3). "Right hand maneuver" means that the right hand does both movements. The wire movement in the "both hands maneuver" pertains primarily to a to-and-fro movement, and in cases where the wire-tip direction needs to be changed or the wire presents the fingers with high resistance, the rotational movement is performed with right hand. In the "right hand maneuver," the wire is advanced by dissecting the tissue with the wire tip (controlled drill). The wire tip is then advanced toward the intentional direction with a sector swing. Either of these approaches is appropriate for CTO-PCI, and each operator will eventually have their own preference. Sometimes, operators use both ways and alter their approach according to the situation of the procedure. Above all, the operator should bear in mind the differences of wire-tip movements with both maneuvers.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 4, NO. 9, 2011
SEPTEMBER 2011:941–51

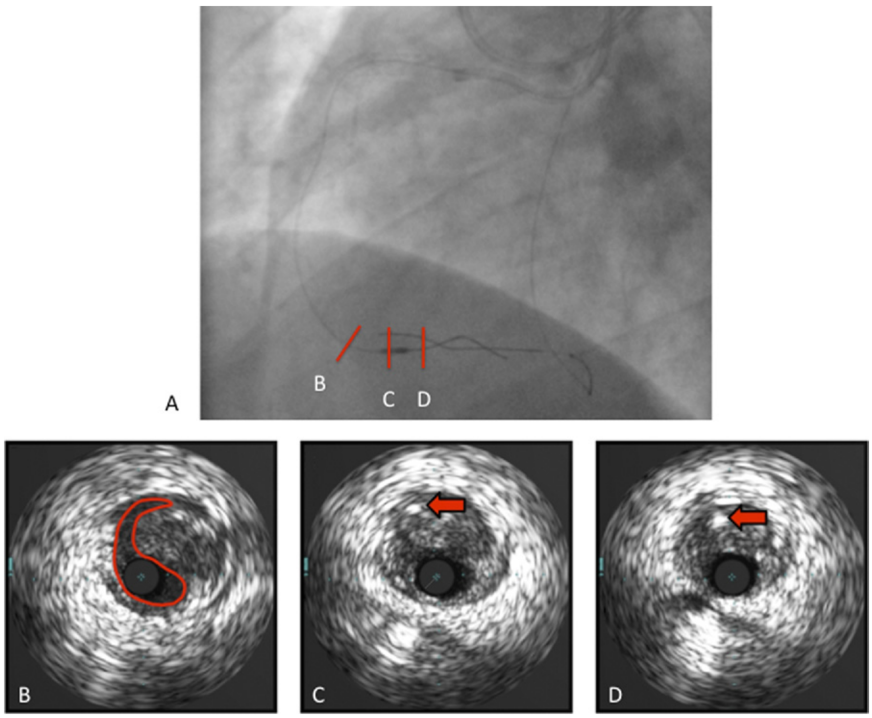

Figure 10. Representative Case of Retrograde Subintimal

On angiography, both antegrade and retrograde wires are apart from each other **(A, D)**, the antegrade ballooning in the subintimal space caused an advanced traverse dissection **(red line in B)**, and the tip of the retrograde wire is located closer to the dissected space created by the antegrade ballooning **(C)**. After this, the retrograde wire communicated easily to the antegrade wire. The **red arrow** indicates the retrograde wire.

Intentional intimal plaque tracking entry point. In the tapered-type entry, the wire is automatically advanced into the appropriate entrance. By contrast, in the abrupt type of entry, it is necessary to look for the dimple sign that is the hallmark of the entry point. At that time, the wire must be manipulated carefully to look for the dimple with the wire-tip trapping trending toward the small hole of dimple. When the operator feels/senses the dimple with the wire tip, the operator should maintain that wire-tip position and then rotate the wire-tip direction 180° to insert the wire tip inside the CTO (Online Video 4).

Intentional intimal plaque tracking of the CTO body. Once the wire tip is inserted into the body of CTO, the operator should advance the wire into the place that is thought to be the intimal plaque, referencing information of other imaging modalities. When the wire is advanced inside the subintimal space on the basis of both angiographic information and data from CT imaging, the wire should be pulled back to the possible position where it initially entered the subintimal space. Next, the direction of wire tip should be turned to continue intimal plaque tracking (Online Video 5). The parallel wire technique—where the original wire cannot be advanced into the true lumen and left there, followed by a second wire being advanced for the intentional intimal plaque tracking—is also useful for intimal plaque tracking. Checking the wire-tip position from several different angiographic angles is very important and essential for confirmation that the wire is inside the intimal plaque.

Intentional intimal plaque tracking exit point. When the wire reaches the exit point of the CTO, the wire should be manipulated finely, gently and carefully for the success of wire crossing. It is very important to control the wire tip intentionally to the direction of the distal true lumen with the examination of the angiogram from several different angles for understanding the relationship with the distal true lumen (Online Video 6). In most cases, once the wire tip is advanced into the distal true lumen, the resistance from the wire tip suddenly becomes lighter, yet it is still very important to confirm that the wire tip is overwrapped on the coronary artery. This confirmation can be done by acquiring angiographic views to confirm that the wire tip can be advanced up to the distal end of the artery without any resistance.

Tactile sensations: "finger feelings" from the wire tip in CTO-PCI. It is often said that "finger feelings" are very important to the success of wire crossing in CTO-PCI. However, this entity is impossible to explain with quantitative parameters and descriptions. This also means that it is virtually impossible to estimate how much wire handling

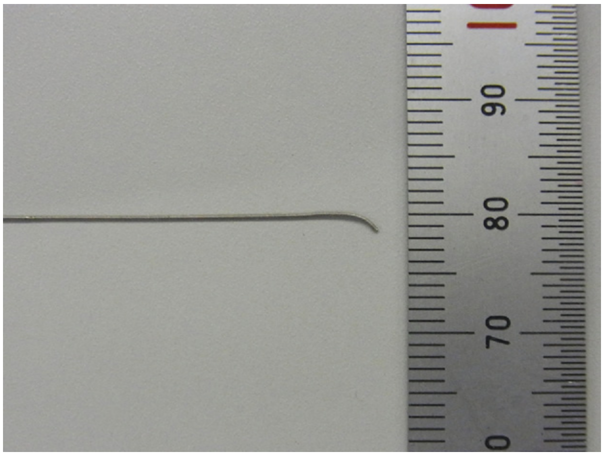

Figure 11. Shape of the Wire Tip in Chronic Total Occlusion Percutaneous Coronary Intervention

A small curve of the wire tip with a 40° to 60° bend at 1 to 2 mm from the tip is made (Online Videos 2, 3, 4, 5, and 6).

feelings and subsequent interpretations contribute to successful crossings. The authors would like to emphasize 3 important feelings that should be focused on during the procedure: 1) the feeling of the dimple at the entry point, especially in the abrupt type of CTO entry, is the key to success, but the dimple does not always guarantee intimal plaque tracking; 2) the feeling of strong resistance when pulling back the wire inside the CTO body, such as when the guide catheter is drawn into it—in this situation, the wire tip has most likely migrated into the subintima; and 3) the feeling of no resistance, and the wire tip moves freely—this most likely means that the wire tip is either in the true lumen or in the extravascular space.

Systematic Strategy for Current CTO-PCI Intervention

The systematic strategy for CTO-PCI procedures helps to clarify this complex treatment technique. Figure 12 shows the current representative step-up strategy of CTO-PCI.

Generally, the Ante is attempted first, and the single wire technique and/or parallel wire technique is used (22). Depending on the lesion type, the Retro will be selected instead of the parallel wire technique. In addition, the Retro might be selected if the Ante approach was unsuccessful (23).

In the Retro, wire advancement to the distal aspect of the CTO lesion through the collateral channel represents the first key step, and this success is just the starting point of the Retro. Usually, after successful wire advancement to the distal CTO, the microcatheter or over-the-wire balloon catheter is advanced to enable an easy wire exchange and better wire manipulation. The Retro usually starts with retrograde wire cross or kissing wire cross, and if these fail, controlled antegrade and retrograde tracking (CART) technique or reverse CART techniques are tried (20,24). Retrograde wire cross can be described as crossing the CTO lesion into the true lumen of the proximal vessel with the retrograde wire (25), whereas kissing wire cross is crossing the CTO lesion into the true lumen of distal vessel with the antegrade wire using the retrograde wire as a landmark (25). The CART technique is performed by first dilating the CTO lesion with the balloon through the retrograde wire, followed by advancement of the antegrade wire into the space dilated with the retrograde balloon (20). The reverse CART technique entails first dilating the CTO lesion with the balloon through the antegrade wire, followed by the retrograde wire being advanced into the space dilated with the antegrade balloon (20). Each technique is further depicted in Figure 13.

To understand the retrograde technique clearly, the authors have classified these strategies into 4 types on the basis of the crossing patterns: 1) determine which wire crossed the CTO, antegrade wire or retrograde wire; and 2) determine whether ballooning was performed for wire crossing. These strategies are addressed in the 2 × 2 contingency table (Table 1). The case of the antegrade wire crossing the CTO lesion without ballooning is done by the kissing wire cross technique. The case where the retrograde wire crosses the CTO lesion without ballooning is done by the retrograde wire cross technique. The case where the antegrade wire crosses the CTO lesion with ballooning is done by the CART technique. Lastly, the case where the retrograde wire crosses the CTO lesion with ballooning is done by the reversed CART technique.

Specific wire techniques for the Retro. For the Retro, the specific wire techniques not used in the Ante are necessary. One is "channel cross," and the other is "retrograde wire externalization."

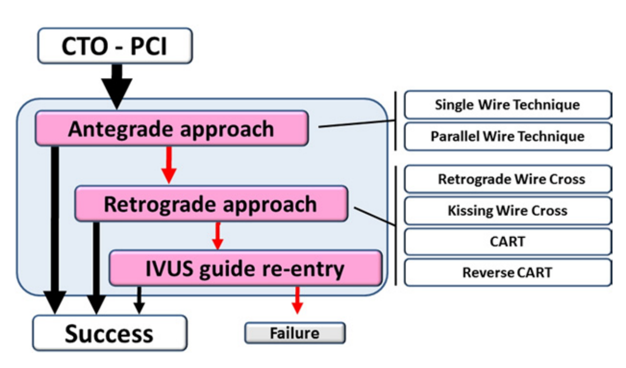

Figure 12. Procedural Steps of Current CTO-PCI

CART = controlled antegrade and retrograde tracking; CTO = chronic total occlusion; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention.

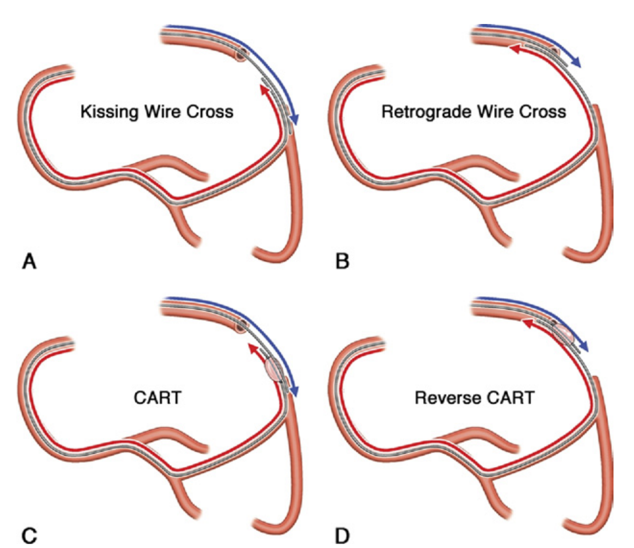

Figure 13. **4 Patterns of Success in Retrograde Wire Technique**

(A) Kissing wire cross. Antegrade wire crosses to distal true lumen while leaving retrograde wire in distal true lumen. **(B)** Retrograde wire cross. Retrograde wire crosses to proximal true lumen. **(C)** Controlled antegrade and retrograde tracking (CART). Antegrade wire crosses to distal true lumen with ballooning chronic total occlusion lesion retrogradely. **(D)** Reverse CART. Retrograde wire crosses to proximal true lumen with ballooning chronic total occlusion lesion antegradely. **Blue arrow line** = antegrade wire, **red arrow line** = retrograde wire.

In the Retro, it is essential to advance the wire and microcatheter though the very tiny channel; thus, the new "channel cross" technique becomes necessary to achieve this. In this way, collateral channels through the septal artery, left and right ventricle epicardial arteries, atrio-ventricle groove, and so forth are used for the delivery of the retrograde wire. In terms of safety and wire deliverability, the septal channel is most recommended (5,26). However, selection of the collateral channel for the Retro depends on performance of the devices, in that, if a new device is introduced, the current selection of collateral channel might change. Specific devices for channel crossing are still under development. Basically, the device should pass through the very tiny channel, so it will at all cost avoid vessel injury with the device. Of note, in the epicardial channel, channel injury might cause cardiac tamponade.

Retrograde wire externalization is also a specific technique. Retrograde wire externalization is helpful in situations where the retrograde wire succeeds in crossing the CTO, as in retrograde wire cross and reverse CART. In these situations, stent implantation is usually impossible even if the wire crosses the CTO, because the stent must be delivered through the tortuous tiny channel in retrograde fashion. Therefore, retrograde wire externalization might be necessary to achieve the desired outcome.

Table 1. **Classification of Retrograde Approach**

	Wire Cross Direction	
	Antegrade	**Retrograde**
Dilation of CTO before wire cross		
No	Kissing wire cross	Retrograde wire cross
Yes	CART	Reverse CART

Draft consensus in Retrograde Summit (Tsuchikane, Ochiai, Sumitsuji).
CART = controlled antegrade and retrograde tracking; CTO = chronic total occlusion.

Steps to retrograde wire externalization are listed as: 1) introduction of retrograde wire into the guide catheter for antegrade entry; 2) retrograde microcatheter or over-the-wire balloon is advanced into the antegrade guide catheter with trapping the retrograde wire inside the antegrade guide catheter with balloon inflation; 3) exchange of the shorter retrograde wire to a longer (300+ cm) wire; 4) longer retrograde wire tip is externalized through the hemostatic valve of the antegrade guide catheter; and 5) from the externalized tip of the longer retrograde wire, the selected PCI device (e.g., balloon, stent) is inserted for delivery into the CTO lesion. Currently, the dedicated long wire for this procedure has been developed; thus retrograde externalization has become safer and easier.

Study limitations. Histopathological studies involving CTO lesions are limited, so currently available histopathological evidence might be insufficient to support our discussion. Wire manipulation is difficult to explain objectively, so descriptions in this manuscript are based primarily on the experiences and opinions of the authors; therefore, this might not be representative of all CTO operators. This review has utility in fostering the understanding of current CTO-PCI. However, as new innovative devices enter this arena, their experience and results will affect interventional aspects of this challenging lesion subset.

Conclusions

Current CTO-PCI techniques and strategies were summarized systematically, coupled with the current histopathological knowledge of CTO. Explanations of wire manipulations and the value of tactile sensations transmitted via the wire along with adjunctive angiographic and imaging data were provided. It is our hope that this article helps interventionalists to better understand this complex procedure in the treatment of patients with CTO to promote safe and efficient results.

Acknowledgment
In the preparation of this manuscript, the authors thank Heidi Bonneau, RN, MS, for her editorial review.

Reprint requests and correspondence: Dr. Satoru Sumitsuji, Osaka University, Department of Cardiology, Nozaki Tokushukai Hospital/Nagoya Tokushukai General Hospital, Bio-L2 Advanced Cardiovascular Therapeutics, Osaka University, 2-2 Yamadaoka Suita, Osaka, 565-0871 Japan. E-mail: sumi2g@sea.plala.or.jp.

REFERENCES

1. Olivari Z, Rubartelli P, Piscione F, et al. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions: data from a multicenter, prospective, observational study (TOAST-GISE). J Am Coll Cardiol 2003;41:1672–8.
2. Prasad A, Rihal CS, Lennon RJ, Wiste HJ, Singh M, Holmes DR Jr. Trends in outcomes after percutaneous coronary intervention for chronic total occlusions: a 25-year experience from the Mayo Clinic. J Am Coll Cardiol 2007;49:1611–8.
3. De Felice F, Fiorilli R, Parma A, et al. 3-year clinical outcome of patients with chronic total occlusion treated with drug-eluting stents. J Am Coll Cardiol 2009;2:1260–5.
4. Rathore S, Matsuo H, Terashima M, et al. Procedural and in-hospital outcomes after percutaneous coronary intervention for chronic total occlusions of coronary arteries 2002–2008: impact of novel guidewire techniques. J Am Coll Cardiol 2009;2:489–97.
5. Rathore S, Katoh O, Matsuo H, et al. Retrograde percutaneous recanalization of chronic total occlusion of the coronary arteries: procedural outcomes and predictors of success in contemporary practice. Circ Cardiovasc Interv 2009;2:124–32.
6. Tsuchikane E, Katoh O, Kimura M, Nasu K, Kinoshita Y, Suzuki T. The first clinical experience with a novel catheter for collateral channel tracking in retrograde approach for chronic coronary total occlusions. J Am Coll Cardiol;3:165–71.
7. Reifart N, Enayat D, Giokoglu K. A novel penetration catheter (Tornus) as bail-out device after balloon failure to recanalise long, old calcified chronic occlusions. EuroIntervention 2008;3:617–21.
8. Srivatsa SS, Edwards WD, Boos CM, et al. Histologic correlates of angiographic chronic total coronary artery occlusions: influence of occlusion duration on neovascular channel patterns and intimal plaque composition. J Am Coll Cardiol 1997;29:955–63.
9. Godino C, Carlino M, Al-Lamee R, Colombo A. Coronary chronic total occlusion. Minerva Cardioangiol 2010;58:41–60.
10. Kragel AH, Reddy SG, Wittes JT, Roberts WC. Morphometric analysis of the composition of atherosclerotic plaques in the four major epicardial coronary arteries in acute myocardial infarction and in sudden coronary death. Circulation 1989;80:1747–56.
11. Katsuragawa M, Fujiwara H, Miyamae M, Sasayama S. Histologic studies in percutaneous transluminal coronary angioplasty for chronic total occlusion: comparison of tapering and abrupt types of occlusion and short and long occluded segments. J Am Coll Cardiol 1993;21:604–11.
12. Munce NR, Strauss BH, Qi X, et al. Intravascular and extravascular microvessel formation in chronic total occlusions a micro-CT imaging study. J Am Coll Cardiol Img 2010;3:797–805.
13. Matsukage T, Masutani M, Yoshimachi F, et al. A prospective multicenter registry of 0.010-inch guidewire and compatible system for chronic total occlusion: the PIKACHU registry. Catheter Cardiovasc Interv 2010;75:1006–12.
14. Ehara M, Terashima M, Kawai M, et al. Impact of multislice computed tomography to estimate difficulty in wire crossing in percutaneous coronary intervention for chronic total occlusion. J Invasive Cardiol 2009;21:575–82.
15. Park Y, Park HS, Jang GL, et al. Intravascular ultrasound guided recanalization of stumpless chronic total occlusion. Int J Cardiol 2011;148:174–8.
16. Rathore S, Katoh O, Tuschikane E, Oida A, Suzuki T, Takase S. A novel modification of the retrograde approach for the recanalization of chronic total occlusion of the coronary arteries intravascular ultrasound-guided reverse controlled antegrade and retrograde tracking. J Am Coll Cardiol;3:155–64.
17. Colombo A, Mikhail GW, Michev I, et al. Treating chronic total occlusions using subintimal tracking and reentry: the STAR technique. Catheter Cardiovasc Interv 2005;64:407–11; discussion 412.
18. Garibaldi S, Godino C, Carlino M, et al. [Treatment of chronic total coronary occlusions by the subintimal tracking and reentry modified technique. The contrast-guided STAR technique]. G Ital Cardiol (Rome) 2010;11:584–9.
19. Brilakis ES, Lombardi WB, Banerjee S. Use of the Stingray guidewire and the Venture catheter for crossing flush coronary chronic total occlusions due to in-stent restenosis. Catheter Cardiovasc Interv 2010;76:391–4.
20. Surmely JF, Tsuchikane E, Katoh O, et al. New concept for CTO recanalization using controlled antegrade and retrograde subintimal tracking: the CART technique. J Invasive Cardiol 2006;18:334–8.
21. Tsujita K, Maehara A, Mintz GS, et al. Intravascular ultrasound comparison of the retrograde versus antegrade approach to percutaneous intervention for chronic total coronary occlusions. J Am Coll Cardiol 2009;2:846–54.
22. Ochiai M, Ashida K, Araki H, Ogata N, Okabayashi H, Obara C. The latest wire technique for chronic total occlusion. Ital Heart J 2005;6:489–93.
23. Barlis P, Di Mario C. Retrograde approach to recanalising coronary chronic total occlusions immediately following a failed conventional attempt. Int J Cardiol 2009;133:e14–7.
24. Kimura M, Katoh O, Tsuchikane E, et al. The efficacy of a bilateral approach for treating lesions with chronic total occlusions the CART (controlled antegrade and retrograde subintimal tracking) registry. J Am Coll Cardiol 2009;2:1135–41.
25. Saito S. Different strategies of retrograde approach in coronary angioplasty for chronic total occlusion. Catheter Cardiovasc Interv 2008;71:8–19.
26. Surmely JF, Katoh O, Tsuchikane E, Nasu K, Suzuki T. Coronary septal collaterals as an access for the retrograde approach in the percutaneous treatment of coronary chronic total occlusions. Catheter Cardiovasc Interv 2007;69:826–32.

Key Words: chronic total occlusion (CTO) ■ histopathology ■ percutaneous coronary intervention (PCI).

APPENDIX

For accompanying videos, please see the online version of this paper.