Current Trend and Techniques of Percutaneous Coronary Intervention for Chronic Total Occlusion

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Contents

1 Clinical Indications of CTO Revascularization

Seung-Whan Lee

1.1 Introduction

Coronary chronic total occlusion (CTO) has been generally defined as complete occlusion of antegrade coronary flow with estimated occlusion for more than 3 months. It has been observed in approximately one-third of patients referred for cardiac catheterization [1, 2]. Over the last decade, percutaneous coronary intervention (PCI) for CTO has rapidly improved and become more generalized despite its technical challenges [3–5]. Development of dedicated guidewires and microcatheters, implementation of new recanalization techniques, and accumulated experience of operators have increased the probability of procedural success and minimized the complication rate [6–8]. Benefits of successful CTO-PCI include reduced angina frequency and improvements in quality of life, left ventricular ejection fraction, or survival [9, 10]. Accordingly, clinical guidelines advocate considering CTO-PCI in patients with selected clinical indications [11, 12]. However, CTO-PCI can lead to procedure-related complications including perforation, myocardial injury, or loss of recruitable collateral flow. Additionally, several studies suggest limited clinical benefit from PCI for well-adopted myocardium to chronic ischemia [13–15]. More importantly, the evidence for CTO-PCI was obtained from observational studies, most of which compared successful and failed CTO-PCI without a control group receiving optimal medical treatment (OMT) [3, 4]. Failed CTO-PCI may be not synonymous with an OMT control group because OMT can avoid inherent complications related to CTO-PCI. Therefore, clinical indications for CTO revascularization, especially focused on CTO-PCI, are very important to drive the decision for an

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attempt. Here we will briefly review cardiovascular outcomes associated with CTO-PCI, and discuss the current guidelines and appropriate use criteria for CTO-PCI.

1.2 Cardiovascular Outcomes of CTO-PCI from Registries and Randomized Trials

Successful CTO-PCI has been associated with numerous cardiovascular benefits, including improvement in left ventricular ejection fraction (LVEF), improved wall motion of the affected segment, and reduction in arrhythmic vulnerability [16–21].

However, it remains undetermined whether CTO-PCI improves left ventricular ejection fraction, risk for arrhythmias, and mortality. Two randomized trials using paired cardiac magnetic resonance imaging, EXPLORE (Evaluating Xience and Left Ventricular Function in PCI on Occlusions After STEMI) and REVASC (Recovery of Left Ventricular Function After Stent Implantation in Chronic Total Occlusion of Coronary Arteries) trial have showed no improvement in LV function [22, 23]. However, in EXPLORE trial, subgroup analysis revealed that patients with CTO located in the left anterior descending coronary artery who were randomized to the CTO-PCI strategy had significantly higher LVEF compared with patients randomized to the OMT strategy (47.2 ± 12.3% vs. 40.4 ± 11.9%; $p = 0.02$). Therefore, in reduced LV dysfunction with CTO patients, CTO-PCI should be used for anyone who has proven large viable myocardium with uncontrolled symptomatic heart failure despite OMT. In terms of arrhythmia, there been no randomized studies examining whether CTO-PCI reduces the risk for subsequent arrhythmias. Relation of ventricular arrhythmia and CTO is not clearly defined, but patients with CTO who received an implantable cardioverter defibrillator for primary or secondary prevention had a higher risk for ventricular arrhythmias than patients with non-CTO coronary artery disease [24, 25] and a higher frequency of recurrent ventricular tachycardia after ablation [26]. Therefore, we need large registry or randomized trial suggesting role of implantable cardioverter defibrillator and CTO-PCI.

Compared to failed CTO-CPI, quality-of-life variables have also been shown to improve after successful CTO-PCI, including improvements in angina, heart failure symptoms, physical activity, and overall treatment satisfaction [9, 27, 28]. Additionally, The EuroCTO (A Randomized Multicentre Trial to Evaluate the Utilization of Revascularization or Optimal Medical Therapy for the Treatment of Chronic Total Coronary Occlusions) multicenter trial randomized 407 patients to CTO-PCI vs. optimal medical therapy alone. At 12 months, compared with patients randomized to medical therapy only, patients randomized to CTO-PCI had greater improvement in angina frequency [subscale change difference: 5.23, 95% confidence interval (CI) 1.75–8.71; $p = 0.003$], and quality of life (subscale change difference: 6.62, 95% CI 1.78–11.46; $p = 0.007$), as assessed with the Seattle Angina Questionnaire [29]. However, the investigators neglected to mention that quality of life, treatment satisfaction, and angina stability were unchanged. Additionally, the single center IMPACTOR-CTO (Impact on Inducible Myocardial Ischemia of PercutAneous Coronary InTervention versus Optimal Medical TheRapy in Patients with Right Coronary Artery Chronic Total Occlusion) trial randomized 94 patients with isolated right coronary artery CTO to CTO-PCI versus OMT alone [30]. At 12 months, compared with OMT, CTO-PCI patients had a significant reduction in ischemic burden and improvement in six-minute walk distance and quality of life as assessed by the short Form-36 Health Survey. However, this trial is single-center experience and analyzed successful PCI versus complaint OMT population among randomized population, which should include all randomized patients such as failed PCI or non-compliant OMT control group. The DECISION-CTO (Optimal Medical Therapy With or Without Stenting For Coronary Chronic Total Occlusion) trial, which was terminated early due to slow enrollment, randomized 417 patients to optimal medical therapy and CTO-PCI and 398 patients to OMT alone. There were no differences in the primary composite outcomes of death, MI, stroke, and any intervention at 4 years or secondary outcomes, including repeat revascularization, mortality at 4 years, or quality of life, as assessed with the Seattle Angina Questionnaire at 3 years [31]. Although there are some limitations of DECISION-CTO trial including the lack of assessment of symptoms once non-CTO lesions were revascularized and the limited assessment for ischemia and viability in the myocardial territories supplied by the CTO, symptom and quality of life assessed with the Seattle Angina Questionnaire gradually improved over times up to 3 years, which means non-CTO PCI with OMT is enough to control symptom and improve quality of life owing to chronic adaptation of collaterals functions supported by OMT over times [31]. Debate on symptom control and quality of life would be clarified by SHINE-CTO trial (SHam-controlled INtErvention to Improve QOL in CTOs—SHINE-CTO; NCT02784418).

Most importantly, successful CTO-PCI versus failed CTO-PCI has been associated with a reduction in all-cause mortality in registry data and meta-analysis [3, 32]. Gao et al. published a meta-analysis of 5958 patients who had undergone successful CTO-PCI and compared them with 1511 patients who had undergone unsuccessful CTO-PCI [21–33]. They found that successful CTO-PCI using drug-eluting stents was associated with lower long-term mortality, lower risk of myocardial infarction, and lower risk of MACCE. The benefits of mortality and clinical outcomes of CTO-PCI were obtained from observational studies, most of which compared successful and failed CTO-PCI without a control group receiving OMT. Furthermore, in an analysis of successful vs. failed CTO-PCI, patients with successful procedures had lower mortality compared with those who had unsuccessful procedures, but findings based on observational studies are subject to bias. In addition, failed CTO-PCI group had significantly higher in-hospital mortality (1.44% versus 0.5%), MI (3.17% versus 2.4%), urgent CABG (4.0% versus 0.5%) coronary perforations, and tamponade. Despite worse baseline characteristics present in unsuccessful PCI patients, not all observational studies are showing worse outcome in the unsuccessful PCI-CTO arm [34]. Periprocedural complications were associated with worse long-term (12 months) health status assessed with the Seattle Angina Questionnaire outcomes and higher mortality (12.4% vs. 3.1%, $p < 0.05$) [35]. There have been 4 randomized control trials to date evaluating CTO-PCI outcomes comparing CTO-PCI versus OMT. DECISION-CTO trial ($n = 834$) showed no difference of 4-year primary composite outcomes of death, MI, stroke, and any revascularization (22.3% vs. 22.4%, hazard ratio, 1.03; 95% CI, 0.77–1.37; $P = 0.86$) and absolutely no benefit in any hard or soft outcomes in the whole population or in any subgroups, including patients with left anterior descending coronary artery CTO, reduced left ventricular function, or acute coronary syndrome up to 4 years [31]. EUROCTO trial ($n = 396$) demonstrated that the cardiovascular event rate at 12 months was comparable with 6.7% in the OMT group and 5.2% in the PCI group [29]. EXPLORE trial ($N = 304$) showed that MACE was not significantly different between both arms (13.5% vs. 12.3%, HR 1.03, 95% CI 0.54 to 1.98; $P = 0.93$) during 3.9 (2.1–5.0) years [36]. Cardiac death was more frequent in the CTO-PCI arm (6.0% vs. 1.0%, $P = 0.02$) with no difference in all-cause mortality (12.9% vs. 6.2%, HR 2.07, 95% CI 0.84 to 5.14; $P = 0.11$) [22]. REVASC trial reported that driven by repeat intervention, major adverse coronary event rates at 12 months were significantly lower in the CTO-PCI group (16.3% vs. 5.9%, $p = 0.02$) [23]. Recently, a meta-analysis of OMT versus CTO-PCI including above 4 random trials and 4 propensity score adjusted registries including 3971 patients showed that no significant differences were found regarding overall MACE, re-PCI, and AMI. Regarding cardiovascular death, CTO-PCI was associated with a better outcome compared with OMT driven by propensity score adjusted registries (OR 0.52, 0.0.81, $P < 0.01$). However, in 4 randomized trials there was no difference in cardiac death [37].

Although previous 4 random trials did not demonstrate clinical benefits of CTO-PCI in terms of cardiac events, those enrolled relatively less symptomatic, preserved LV function patients and less complex CTO patients (JCTO score ranging 1.67–2.2, SYNTAX score ranging 14–29). Furthermore, the prognosis of CTO patients may differ based on the amount of myocardium at risk that is subtended by the CTO vessel and this should be a subject of investigation. Therefore, clinical trials comparing optimal medical therapy and CTO-PCI versus optimal medical therapy alone are therefore still needed in higher risk patients with more complex CTOs and/or large to medium sized ischemia, but investigators should be cautious because investigators face significant difficulties, including high cost to conduct randomized control trials, unexpected complications, barriers to randomize patients who are highly symptomatic, crossovers, and the relative high PCI failure in complex CTO.

1.3 Current Guidelines

The 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention recommended CTO-PCI in patients with clinical indications and suitable anatomy when performed by operators with appropriate expertise (Class IIa, Level of Evidence [LOE] B) [11].

The 2014 European Society of Cardiology and European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization recommend CTO-PCI to be considered in patients with expected ischemia reduction in a corresponding myocardial territory and/or angina relief (Class IIa, LOE B). They recommend an initial anterograde approach and consideration of a retrograde approach if this fails or a primary retrograde approach in selected patients (Class IIb, LOE C) [12].

The ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease have eliminated the separate criteria for CTO lesions as was the case in the 2012 guidelines. Currently, indications for revascularization in SIHD are determined irrespective of whether the lesion is a CTO [38]. The indication for revascularization of a coronary artery lesion, whether CTO or severe stenosis, is based on symptoms, the extent of antianginal medications, and the risk of ischemia.

1.4 Conclusions

Previous numerous registries and meta-analysis comparing successful vs. unsuccessful PCI support CTO-PCI for benefit of mortality and cardiac outcomes, which was not demonstrated in randomized trials. Despite discordant quality of life outcomes from DECISION-CTO and EUROCTO trial, symptomatic benefit can be achieved by alleviating ischemia in symptomatic patients (chest pain or dyspnea) after OMT. Therefore, patients who have symptoms of ischemia despite optimal medical therapy with viable myocardium are likely to gain the most benefit from CTO-PCI. The procedural benefit will likely be proportional to symptoms severity. Therefore, informed discussions with patients and providers emphasizing the risk and benefits associated with CTO-PCI for a given patient's condition are the keys to providing patients with appropriate CTO-PCI. From technical point of view, CTO-PCI continued to evolve and achieve maturation of non-occlusive coronary artery disease PCI. Therefore, the CTO-PCI deserves and should be reserved for proper indication.

Conflict of Interest Statement The authors have no conflicts of interest to declare.

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2 CTO PCI in Clinical Readings of Angiography

Sunao Nakamura

2.1 Introduction

The most important mission of percutaneous coronary intervention (PCI) of chronic total occlusive (CTO) lesion is to provide clinically successful recanalization. Sufficient preparation prior to the procedure is essential for the successful recanalization since CTO PCI is the most technically challenging. In this regard, how well the coronary angiogram is interpreted is the first and foremost step in the procedure. In this chapter, clinical reading of angiogram is discussed focusing on pragmatic and practical aspects.

2.2 General Occlusion Pattern of CTO

Each coronary artery has its own general pattern of occlusion which was elucidated by Levine DC already in 1974 presented in Circulation [1]. Those patterns are illustrated in Fig. 2.1a–c. Author based on his experience agrees to these schema. Among these CTO lesion, depending on its occlusive pattern, some are easy and some are extremely difficult to recanalize. JCTO score developed by Morino et al. [2] is useful to classify lesion by procedure difficulty (Fig. 2.2).

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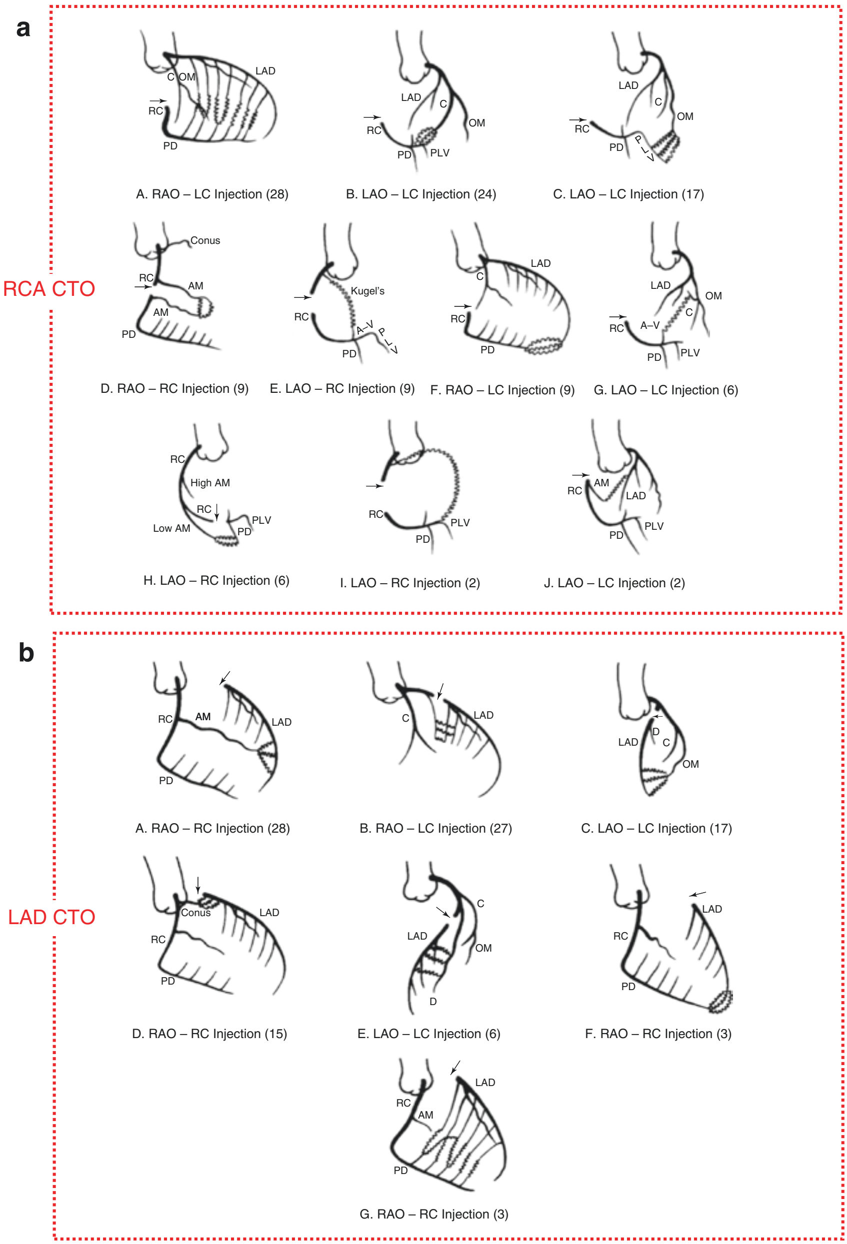

Fig. 2.1 Topography of collaterals and collateral function in coronary artery occlusion. (**a**) Right coronary artery occlusion(RCA); (**b**) circumflex coronary artery(LCX); (**c**) left anterior descending coronary artery (LAD). *AM* acute marginal branch of the right coronary artery, *A-V* artery to atrioventricular node, *D* diagonal branch of the left anterior descending, *LAO* left anterior oblique, *LC* left coronary artery, *OM* obtuse marginal branch of the circumflex artery, *PD* posterior descending branch of right coronary artery, *PLV* posterior left ventricular branch of the right coronary artery, *RAO* right anterior oblique

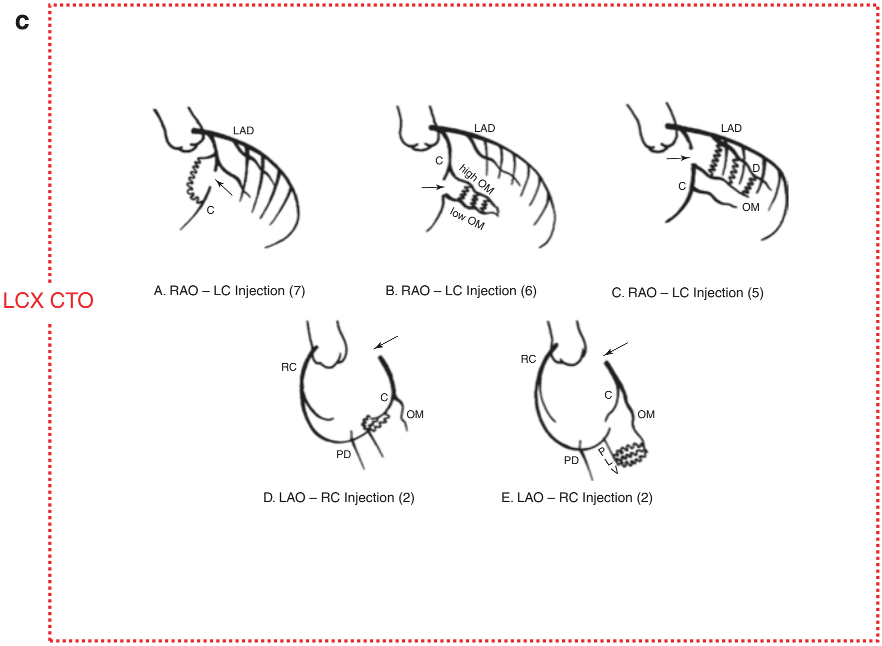

Fig. 2.1 (continued)

It is not too much to say that recent CTO PCI technique has been well developed and matured. By combining antegrade approach, in which lesion is accessed from proximal side and retrograde approach, in which lesion is accessed via collateral vessel, 80–90% of CTO cases are successfully revascularized. This is because retrograde approach is quite reliable technique which is described in other chapter (Fig. 2.3).

2.3 Grasping the Level of Difficulty from Angiogram

As shown in Fig. 2.3, most of the current CTO PCI cases have reserve of retrograde approach as backup. Accordingly, degree of difficulty of CTO PCI is determined by the combination of JCTO score which shows the difficulty in antegrade approach presented by Morino et al. [2] and J channel score indicating the difficulty level in retrograde channel crossing through several types of collateral reported by Nagamatsu et al. [3] (Fig. 2.4). Therefore angiogram examination prior to the CTO PCI procedure should cover to evaluate both occlusion side and collateral circulation side. What is important in clinical reading of coronary angiogram prior to PCI is consideration by combining of findings from occlusion side and collateral circulation side. Typical case showing the importance of both evaluation is shown below (Fig. 2.5).

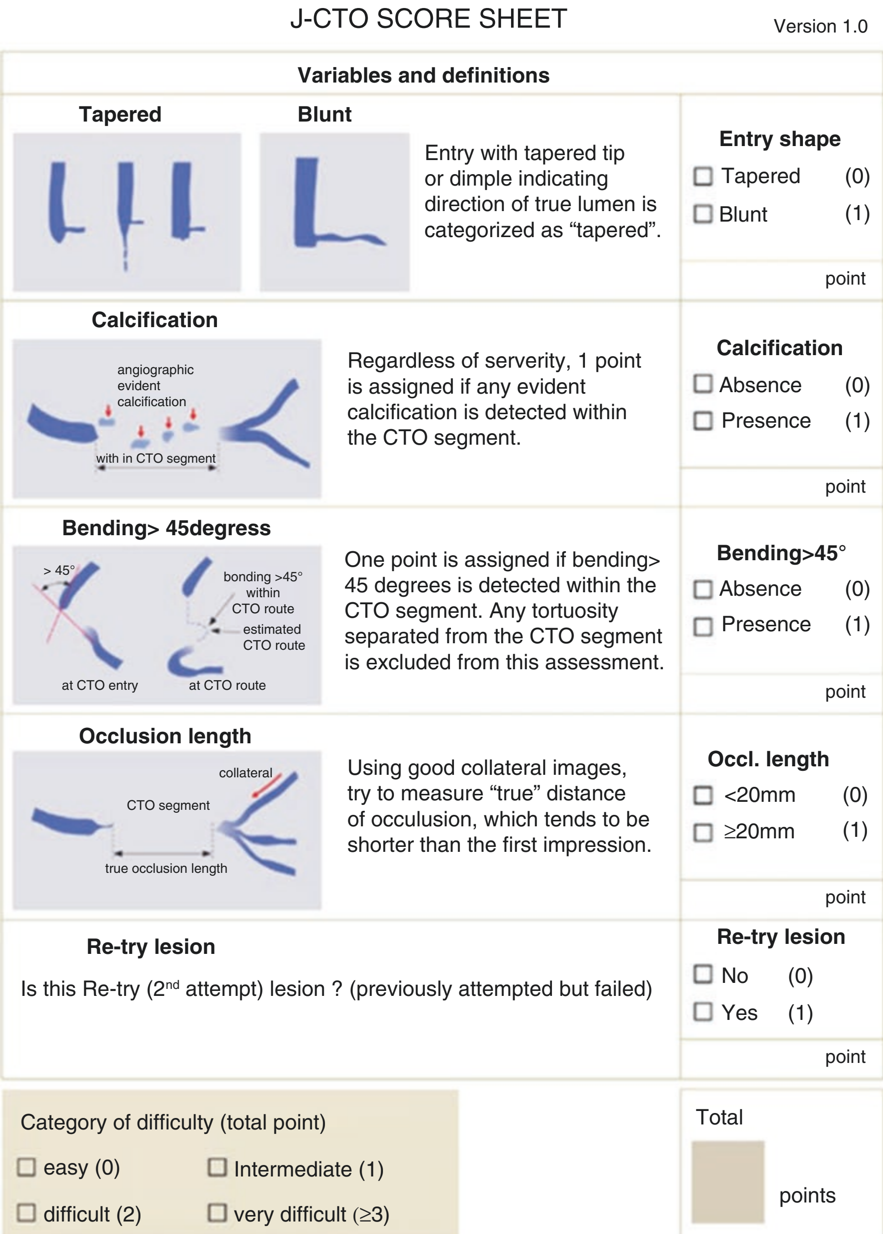

Fig. 2.2 Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 min: the J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. Morino Y, Abe M, Morimoto T, JACC cardiovasc Interv 2011 Feb;4(2) 213–221

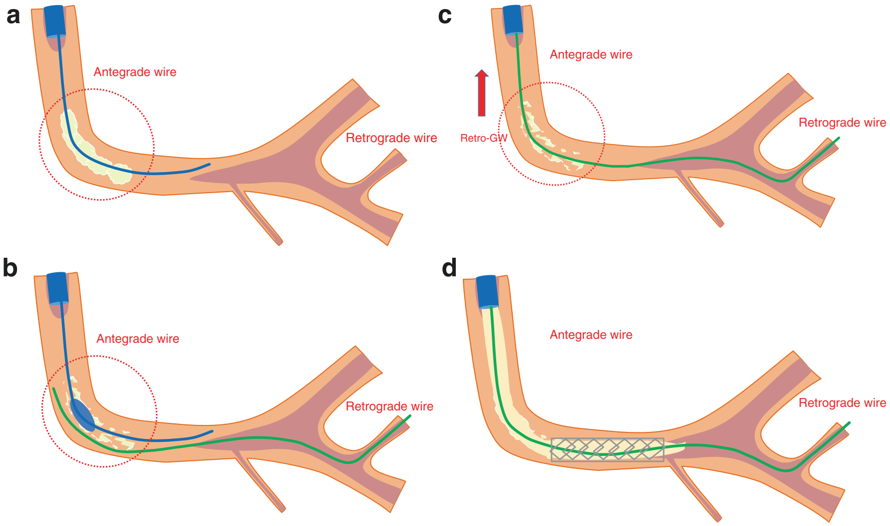

Fig. 2.3 In case of difficulty of antegrade success, we consider "retrograde option" (**a**). Once retrograde guidewire track into collateral circulation, need to advance into it in CTO proximal as far as possible. Then ballooning from antegrade manner to make communication space between antegrade and retrograde (**b**). Then retrograde guidewire passes through this space and creeping up to the antegrade guide catheter, we can finish externalization (**c**). Finally, ballooning and stenting from antegrade manner (**d**)

This is LAD CTO case whose occlusion starting point is unclear, the so-called no stump CTO case. This is a highly complicated and very difficult case in antegrade approach. Even such a high point difficult case, angiogram of collateral circulation shows that there is a small and bending collateral extended from RCA to LAD. If this channel is selected and a retrograde wire is advanced through all the collateral lesion, into the LAD, and close enough to LAD proximal, this tough case is instantaneously reversed to be a very promising case. Advancing the retrograde guidewire close to the starting point of occlusion allowed antegrade guidewire was bringing in LAD, then advance and by kissing wire technique it reached to distal of the lesion. Ballooning and stenting were done from antegrade approach to complete the case. As this case shows, thorough examination of both occluded lesion side and circulation providing collateral side angiogram is basis. As a matter of course, clear and optimum angiogram prior to the procedure is necessary which allow operators to plan strategy of the procedure.

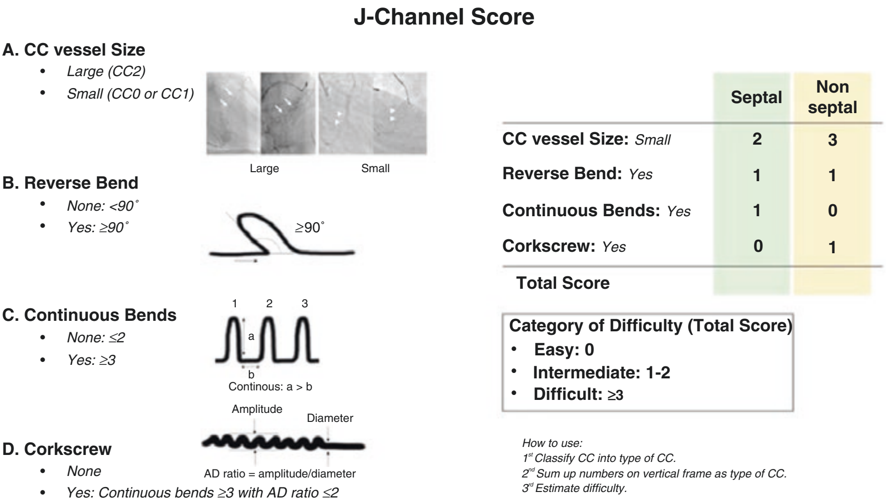

Fig. 2.4 Predicting successful guidewire crossing via collateral channel at retrograde percutaneous coronary intervention for chronic total occlusion: The J-channel score as a difficulty estimating tool for collateral channel guidewire crossing success from the Japanese CTO-PCI Expert Registry. EuroIntervention 2019 Apr 23. Nagamatsu W, tsutikane E, Oikawa Y, Katoh O

2.4 Optimum Plane and Its Selection in Angiogram Observation

2.4.1 Right Coronary Artery CTO

2.4.1.1 Consideration from Antegrade Approach

It is significant to know about the running route of RCA. From the origin of RCA in the proximal to the ostium, it runs horizontally and right after the origin, it also leans slightly backward to run between atrium and ventricle passing through the bottom of the heart toward left ventricle. What is most unique to RCA is that it splits into AV side and PD side. When RCA CTO is recanalized, as it is known, unless sufficient flow is regained for both branches, long-term patency cannot be expected. With this kind knowledge on RCA, it is important to create a setting of appropriate fluoroscopic views, namely LAO 45°+RAO view, AP caudal view, or AP cranial view to observe the lesion from orthogonal two different planes (Fig. 2.6 RCA).

2.4.1.2 Consideration from Retrograde Approach

Entering and crossing the collateral branches for retrograde approach is discussed in other chapter. In many cases, they are originated from LAD septal branch. In other cases, they are developed from epicardial channel from LAD distal, epicardial channel from CX, or some are developed via atrioventricular groove channel. Identification of most appropriate channel for retrograde approach is the key for success.

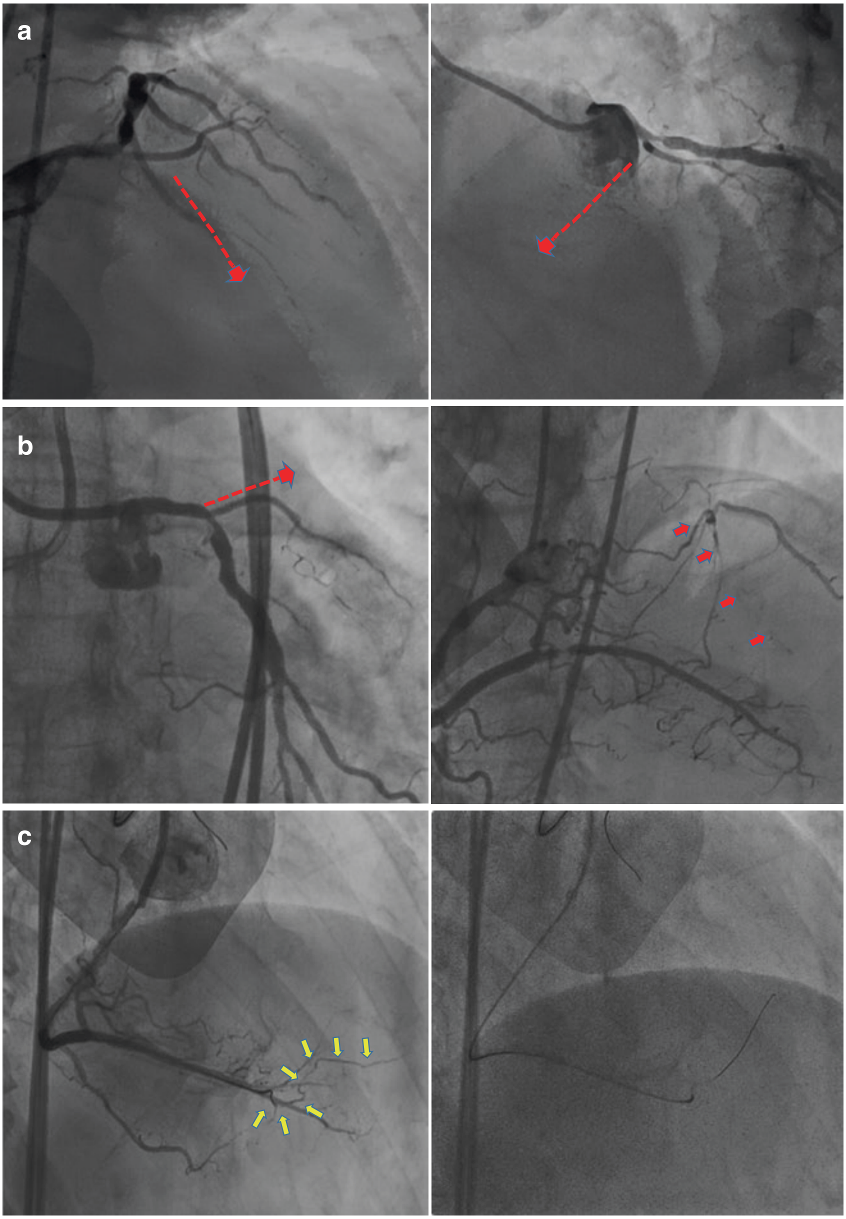

Fig. 2.5 A case of LAD no stump CTO with severe stenosis in LCX ostium (**a**). We checked several view to recognize the guidewire position. Then realized collateral from conus branch and distal RCA (very faint collateral) (**b**). After starting some antegrade preparation, because of the difficulty of antegrade, the, started retrograde A, we could see clearly but tortuous collateral from PD branch and LAD. Following small tiny tortuous collateral, GW is creeping up toward LAD with respect of some deep bending area (**c**). Advancing Corsair pro as deep as we could. Then started ("Approaching both GW" and wants "KISSING Wire.") (**d**). Then the Corsair pro is also creeping up LAD. (**c**) So we started ballooning and stenting all the way down to the LAD distal. After treating LAD/Dx bifurcation area with appropriate KBT, we did LMT~LAD +LCX TAP stenting. Then we did POT in LMT ost. And KBT in LAD/LCX (**e**)

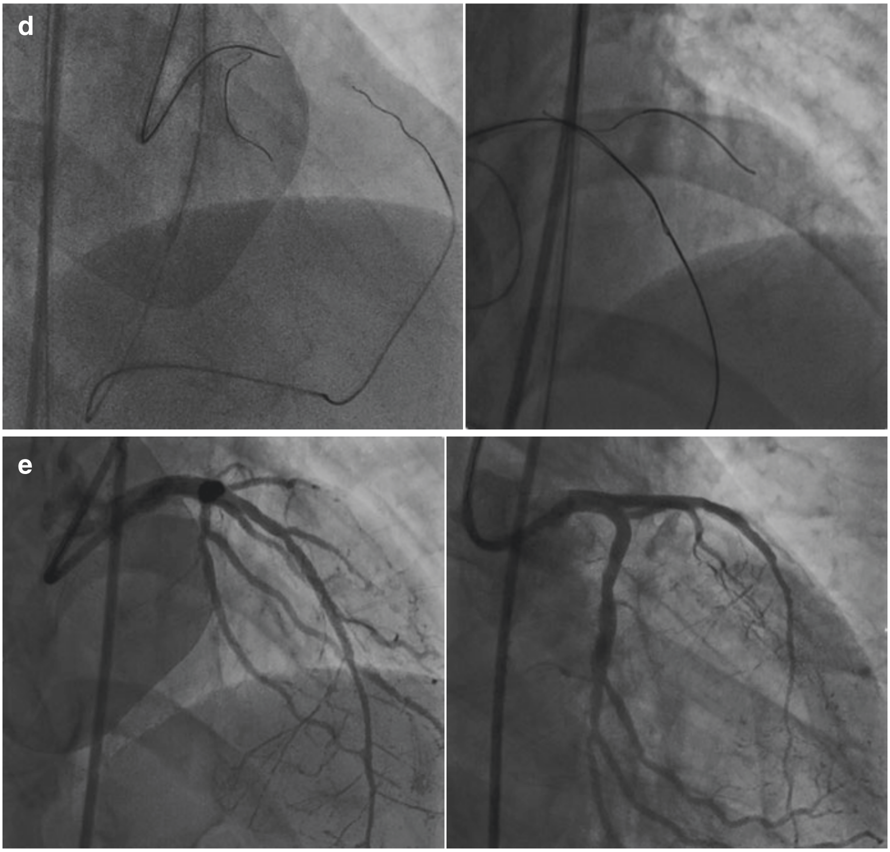

Fig. 2.5 (continued)

2.4.2 Left Anterior Descending Coronary Artery CTO

2.4.2.1 Consideration from Antegrade Approach

LAD branched off from left main coronary artery extends to the anterior surface toward downward with gradually oval shape. Its starting angle is determined by the size of left circumflex artery and their bifurcation angle. When the first diagonal artery is branched off LAD is affected for its angulation from where it runs downward along the surface of egg-shape heart all the way to the bottom of the heart drawing a mild curve. Tracing this anatomy in the mind and observing the optimum orthogonal 2 planes, guidewire is advanced. Two views are chosen from LAO 40° AP cranial, RAO cranial, 90° lateral and Spider view (Fig. 2.6 LAD a,b,c,d,e).

2.4.2.2 Consideration from Retrograde Approach

Collateral in some cases develops from circumflex which is dominant vessel but in most cases it develops from RCA distal. In general proximal septal branches are easy to use for retrograde approach. For the purpose of establishing the evidence, it is expected to evaluate its success ratio by referring to J channel score reported by Nagamatsu et al. [3]. This point is also elaborated in different chapter.

2.4.3 Left Circumflex Coronary Artery CTO

After branching off from left main coronary artery, left circumflex extends oblique downward developing side branches to cover lateral surface of the heart. Many of its occlusion occurs at proximal part involving its distal bifurcation lesion. Its occlusive lesion is on three-dimensional curve which is unpredictable whose radius of curvature is unique to each patient. This is one of the causes that the PCI success ratio in LCX is lower than LAD and RCA PCI. This is also the reason for overestimation of vessel diameter on angiogram which may lead to implant a larger stent to cause perforation or rupture of the vessel. Recommended angiogram view planes are RAO30°, AP caudal view, RAO30° caudal view, Spider View, LAO30° Cranial30° view (Fig. 2.6 LCX).

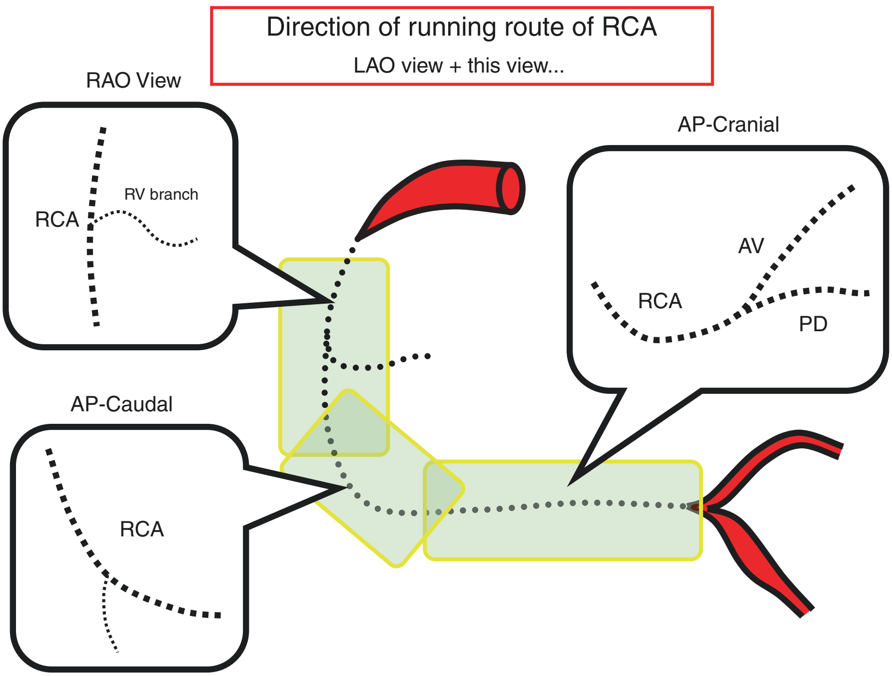

Fig. 2.6 (RCA)

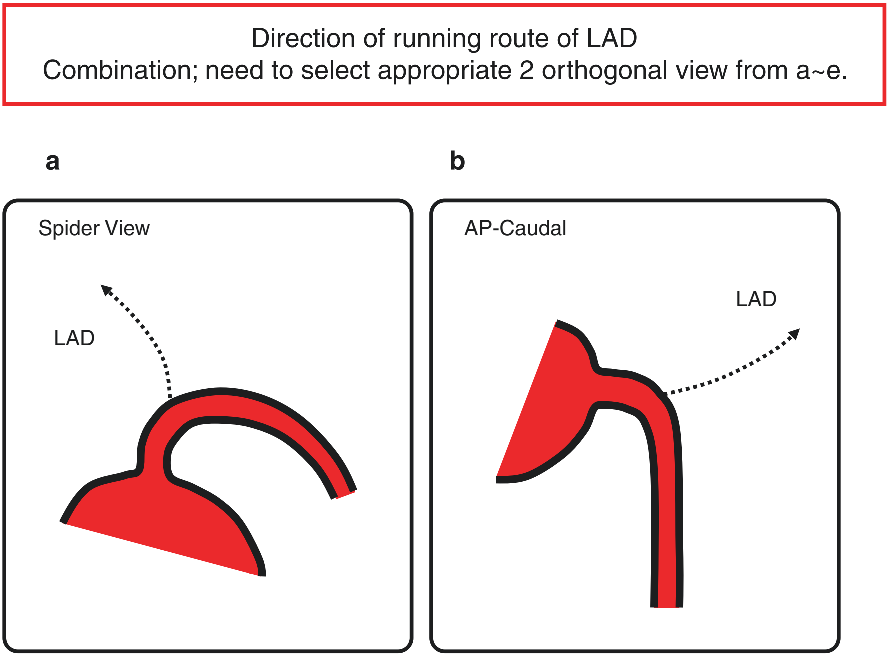

Fig. 2.6 (continued)

2.4.3.1 Consideration from Retrograde Approach

Collateral circulation can be developed from any vessel. Sufficient examination should be given to identify promising collaterals.

2.5 Complementing Modality to Coronary Angiogram

The ultra-right wing is the most prevailed coronary CT. There is no doubt for its utility. Figure 2.7 shows very detail depiction of coronary artery path provides with much more information though the CTO looks very complicated on angiogram. There is no choice not to utilize coronary CT. Figure 2.8 shows RCA CTO. Occlusion length is not so long. However, bending in the CTO lesion is not known (Fig. 2.8a, b). It is apparent that mono-antegrade approach does not solve the problem. Coronary CT image prior to the procedure would give us much more information (Fig. 2.8c). This is a tool to provide intraluminal information which is a very powerful weapon for PCI.

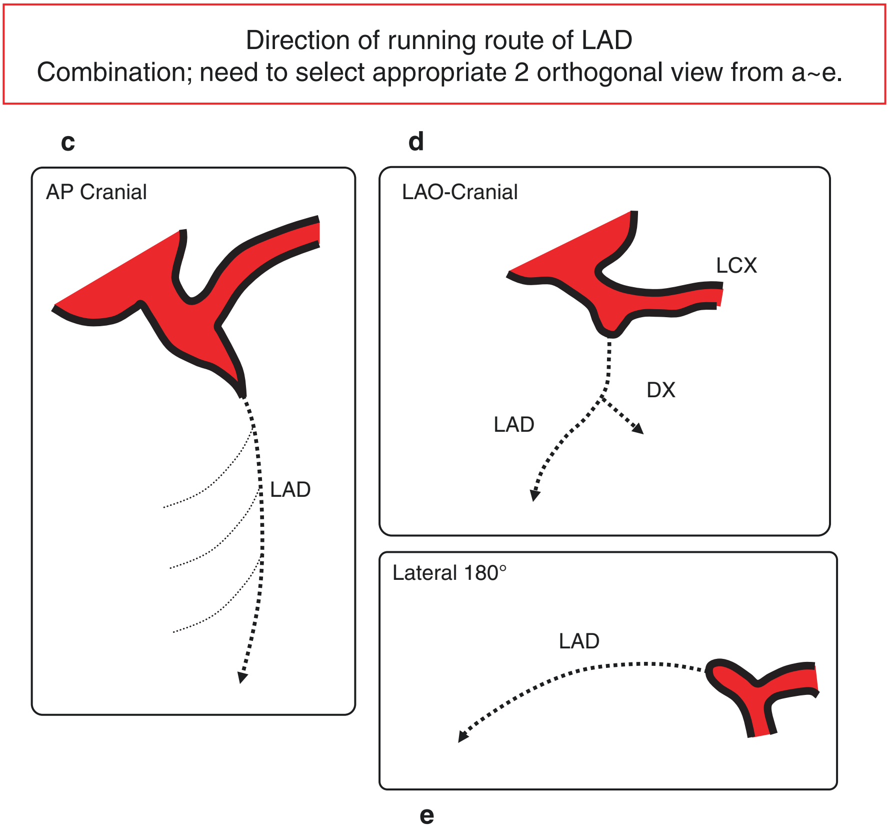

Fig. 2.6 (continued)

Physical parameters for cardiac function are also useful in deducing critical information. Even assuming that angiogram indicates long CTO lesion, if the patient's left ventricular ejection fraction is normal, most of these cases turn out that occlusion length is not long. When left ventricular function is normal, generally side branches are alive. In this manner, not only image diagnosis but also clinical characteristics would allow the operator to deduce the structure of the CTO lesion.

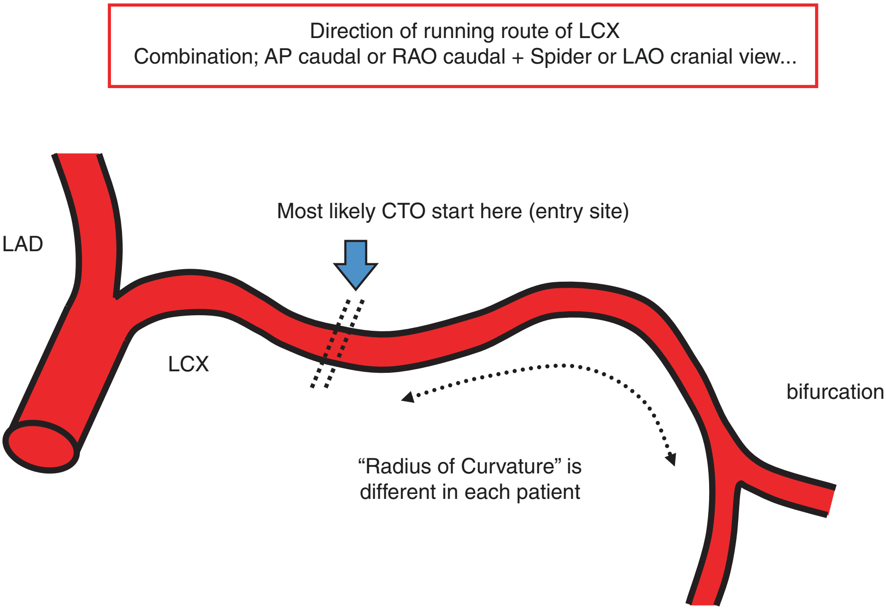

Fig. 2.6 (continued)

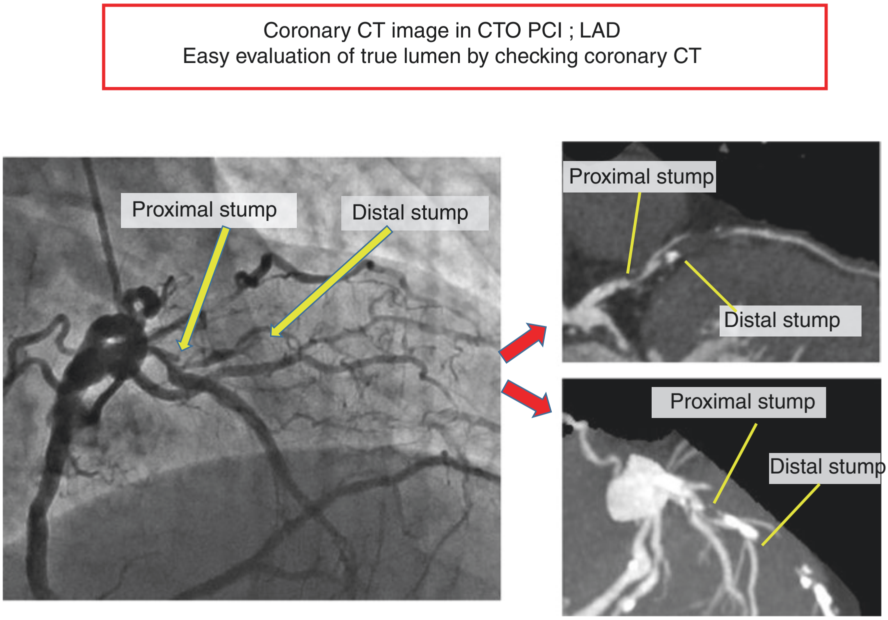

Fig. 2.7 Left Panel: angiogram of chronic total occlusion in left anterior descending artery. Yellow arrows indicate the position of both proximal stump and distal stump. Right panel: coronary CT images in different angle. Yellow arrow indicate the position of proximal and distal stump. Coronary CT image clearly shows proximal connect distal left anterior descending artery

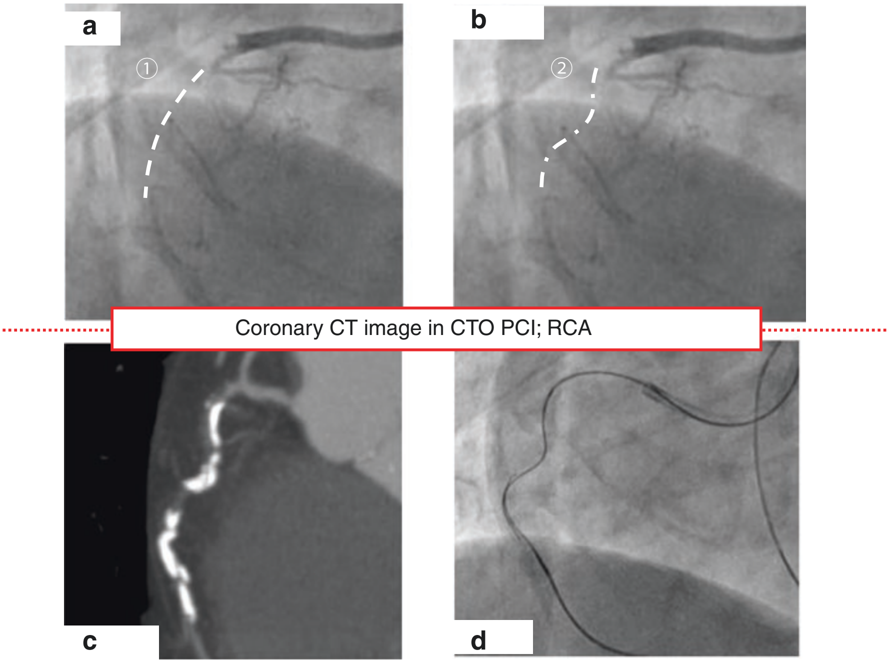

Fig. 2.8 Upper panel: angiogram of chronic total occlusion in right coronary artery. (**a**) and (**b**) show two virtual broken line which is very difficult to identify. (**c**) coronary CT image in this case which clearly shows the right path in chronic total occlusion. (**d**) After guide wiring from antegrade and retrograde, both guide wires meet in right position of chronic total occlusion. Whole line of guide wires shows similar image of coronary CT

2.6 Summary

It is no exaggeration to say that the key for success for CTO PCI is how much in detail that the case is studied before the procedure. As was discussed in this chapter, surpassing knowledge on basic anatomical characteristics of each coronary artery will be a great help for the operator. As an example collateral vessels develop by following their anatomical rules. Such physiological and anatomical knowledge would be a great help in CTO PCI procedure. When guidewire is advanced, no matter what, its position should be checked always from two orthogonal view planes so that three-dimensional position of the guidewire is verified. This basic rule would prevent the operator from causing coronary artery puncture. The strongest defense from complications is not to cause any from the very beginning. Author strongly hope that every PCI operator enjoys high success rate without causing any complication with sufficient knowledge and intelligence.

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3 Trends in CTO-PCI Dedicated Intravascular Ultrasound

Junichi Yamaguchi

3.1 Introduction

Previously, intravascular ultrasound (IVUS) catheters had large diameters and a long distance between the tip and the transducer, which limited their usefulness in percutaneous coronary intervention (PCI) for chronic total occlusion (CTO). Recently, a new IVUS catheter has been introduced, with a smaller diameter and a shorter distance between the tip and the transducer. Since then, this improved IVUS catheter has been used in various situations in CTO-PCI. The specific uses of IVUS in PCI for CTO include:

(1) Assessing the condition of angiographically undetectable vessels
(2) Confirming the route of a guidewire passing through CTO without cineangiography.

This chapter describes the use of IVUS in PCI for CTO.

3.2 Operation Using Antegrade Approach

For simultaneous wiring using IVUS guidance, it is desirable to set the antegrade system to 7 Fr or more. When the antegrade guide is an 8 Fr catheter, wiring to the site of CTO is possible, even if the IVUS catheter is positioned in the side branch of the affected coronary artery.

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3.2.1 Search for the Entry Point from the Side Branch

In this approach, angiography-guided antegrade wiring is usually initiated in patients with a taperd-type entry of CTO that is more easily identifiable. However, in patients with a blunt-type entry of CTO, it is often hard to identify the exact point of CTO entry. In such cases, the position of CTO entry may be identified by inserting the IVUS catheter into the side branch of the occluded coronary artery, provided the side branch (which may occasionally be the main vessel) is present at the site of the blunt-type obstruction. These approaches might be made in all cases except for the entry of the left main trunk (LMT) and the entry of the right coronary artery (RCA).

The IVUS catheter is inserted into the side branch and pull-back is performed by manual manipulation while confirming a live image. The entry of CTO can often be found in an area with an increased diameter of the side branch vessel; this area should be carefully observed to identify the site of entry. In cases where it is difficult to insert the IVUS catheter into the side branch and the catheter is made to enter from the proximal area for observation, the entry of CTO may often be present in an area where the vessel diameter is small. If the entry of CTO can be identified, it is important to record the position of the IVUS catheter using cine angiography for reference during wiring. In patients with calcification of the entry and occluded vessels behind the calcification, it may be difficult to identify the point of entry even if the IVUS catheter is used. By changing the depth and gain settings of the catheter, the entry of CTO may become observable.

Currently, various types of IVUS catheters are available. However, the position of the transducer on the catheter may vary depending on IVUS. Therefore, confirming the position of each transducer according to the IVUS catheter is required.

When wiring is initiated by antegrade approach and the guidewire is inserted 5–10 mm into the occluded vessel after having identified the blunt-type entry of CTO in IVUS, it is desirable to confirm whether the wire has entered from the assumed entry by performing IVUS from the side branch again. The steps to identify the route of the guidewire inserted into CTO are as follows:

(1) Confirm whether the guidewire is present inside the blood vessel at the entry of CTO
(2) Confirm the positional relationship between the side branch bifurcation and the guidewire
(3) Confirm whether the guidewire is positioned at the center of the occluded vessel using short axis view

3.2.2 IVUS-Guided Rewiring in Antegrade Approach

IVUS-guided rewiring is a procedure that identifies the true lumen of the vessel by inserting a second wire from the subintimal space along with inserting a guidewire under IVUS guidance. This procedure is used in cases where the guidewire cannot aim at the true lumen and instead locates the CTO entry point in the subintimal space. It is used as a last resort when the guidewire cannot be inserted into the true distal lumen after trying various methods such as antegrade parallel-wire technique and retrograde approach.

It is essential to understand that IVUS-guided rewiring is not a technique for re-entry of the wire into the true lumen from the subintimal space. Even if the true lumen can be confirmed in IVUS, it is structurally and physically challenging to penetrate it by inserting the second wire from inside the subintimal space. Therefore, the site where the second wire is guided into the true lumen (intimal space) should either be the site of aberration created when the first wire entered into the subintimal space or a site that is moderately proximal to it. Thus, the most important thing is to confirm the position of aberration of the first wire on angiography or IVUS and to confirm the position and direction of the true lumen on IVUS under fluoroscopy imaging.

For the insertion of the IVUS catheter into the subintimal space, it is important, as far as possible, to make an effort not to enlarge the subintimal space. A micro-catheter may be inserted into the subintimal space first, after which passing the IVUS catheter may be easier. In spite of this, if it is still hard to insert the IVUS catheter into the subintimal space, the subintimal space can be dilated incrementally using a 1.5 mm balloon. Figure 3.1 shows the findings of IVUS in a case where the guidewire entered the subintimal space; A: both the first and second wires are located in the true lumen, B: both the first and second wires are located in the intimal space, C: the first wire is located in the subintimal space and the second wire is located in the intimal space, D: the first wire is located in the subintimal space, the second wire is located in the intimal space, and the true distal lumen can be confirmed, E: the first wire is located in the subintimal space and the second wire is located in the true distal lumen. The steps of IVUS-guided rewiring are as follows:

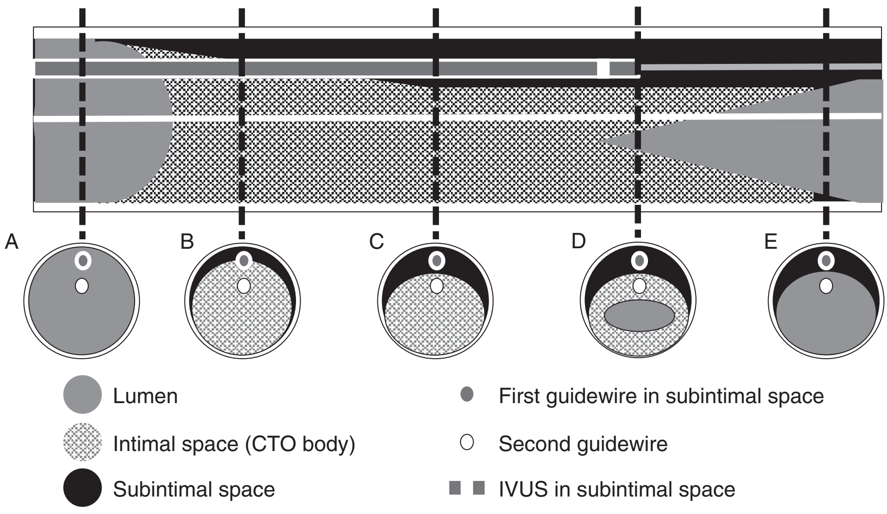

Fig. 3.1 Images during antegrade IVUS-guided rewiring

(1) Identify Part B by IVUS, and then try to penetrate the CTO using the second wire from the site between Part A and B which is different from the site of the first IVUS guidewire
(2) Insert the second wire carefully while confirming that it is located in the intimal space using the IVUS image obtained from the subintimal space by the first wire. *An important consideration during this step is to understand that the direction that the guidewire should be originally advanced in is positioned on the short axis view of the distal part. The direction that the second wire should be advanced in is the area of the plaque as seen on short axis view.*
(3) Try to identify the true lumen using the second wire by confirming the position that indicates the true distal lumen as seen on the IVUS image obtained from the subintimal space by the first wire. When the condition of Part D is achieved, changing the direction by pulling the second wire may be effective occasionally.
(4) Finally, make sure that the condition of Part E is achieved.

Once you can understand in which direction the IVUS image corresponds to fluoroscopy imaging, the insertion of the guidewire is enabled under fluoroscopy. Therefore, first, insert both the IVUS catheter and the second wire into the subintimal space to align the plaque, IVUS catheter, and guidewire into a linear shape; then, angle them such that the longest possible distance between the IVUS catheter and the guidewire. This orientation is applied to visualize the straight line linking the plaque, the IVUS catheter, and the guidewire from the side under fluoroscopy. Once the guidewire is advanced to the other side of the IVUS catheter, it can be guided into the plaque. An alternative approach includes confirming the positional relationship of the occluded artery with the branch, confirming the state of the epicardium, and using wire bias and lumen bias. It is useful to estimate the direction of the catheter and the guidewire on IVUS corresponding to fluoroscopy imaging by using these approaches as much as possible.

For the second wire, it is better to choose a wire with a higher torque transmission than that of the first wire and with an increased penetration ability. Currently, GaiaNext2 or Next3 is often chosen, and Conquest Pro is also used in some cases. To avoid re-aberration of the guidewire into the subintimal space once it is inserted into the plaque, consider performing step down of the wire if the microcatheter can be inserted into CTO.

3.3 Utilization of IVUS After Retrograde Approach

Recently for retrograde CTO-PCI, the reverse CART approach for the guidance of the retrograde guidewire into the true proximal lumen has been chosen in many cases. However, even if antegrade balloon dilatation is repeated, the retrograde guidewire cannot often reach the true proximal lumen. In such a case, confirmation of the positional relationship between the antegrade and retrograde guidewires

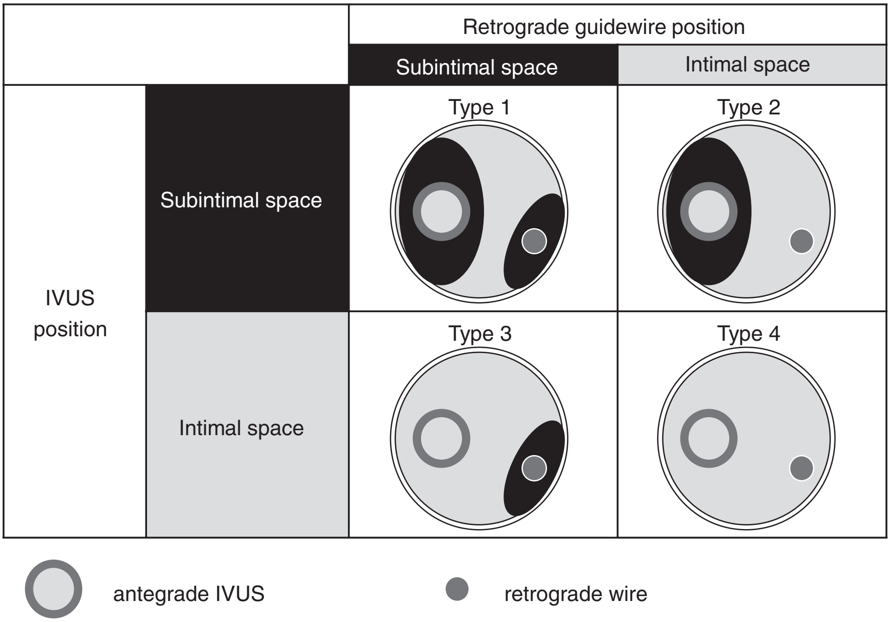

Fig. 3.2 IVUS findings from antegrade guidewire during reverse CART procedure

using IVUS may be useful to resolve the issue. Navifocus WR (Terumo Medtronic) or Eagle Eye (Volcano Corporation), both of which have a short distance between the catheter tip and the transducer, are recommended for use as IVUS catheters. Unless there is severe calcification, the positional relationship between the antegrade and retrograde guidewires can be identified by inserting the IVUS catheter. Each wire will be present either in the intimal space or the subintimal space, and there are four patterns in this relationship (Fig. 3.2).

3.3.1 Type 1: Both the Antegrade IVUS Catheter and the Retrograde Guidewire Are Located in the Subintimal Space

In such a case, it is relatively easy to create a connection by the reverse CART approach depending on the length of the occlusion. The communication between the subintimal spaces is established by antegrade dilation of the balloon, which is almost the same size as the blood vessel diameter measured by IVUS. The communication is relatively easy to establish even if there is a large distance between the antegrade IVUS catheter and retrograde wire because subintimal spaces are usually oriented in a spiral. If no communication can be established, it may often be necessary to choose a larger balloon. It may also be useful to choose a retrograde wire with a flexible and smooth tip.

3.3.2 Type 2: The Antegrade IVUS Catheter Is Located in the Subintimal Space and the Retrograde Guidewire Is Located in the Intimal Space

As compared to the other three types, this pattern is often hard to achieve by the reverse CART approach. Dilatation of the antegrade balloon usually only results in enlargement of the subintimal space. However, in some cases, the true proximal lumen can be accessed by retrogradely inserting a wire with high penetration ability and control (e.g., GaiaNext2/3) toward a balloon with a relatively small diameter intentionally during its deflation (contemporary reverse CART).

In IVUS, it is required to develop a strategy depending on the situation. For example, the usual reverse CART approach can be used by guiding the wire into the subintimal space by intentionally trying to change the position for trial reverse CART approach or by switching the retrograde wire into the knuckle wire, in which case it can be penetrated toward the direction of dilation of the balloon at a sharp angle using a stiff wire such as Conquest Pro.

3.3.3 Type 3: The Antegrade IVUS Catheter Is Located in the Intimal Space and the Retrograde Guidewire Is Located in the Subintimal Space

In this type, the procedure is similar to the Type 1 procedure, theoretically. By antegrade dilation of a large balloon, which is almost the same size as the blood vessel diameter, a crack leading to the subintimal space from the intimal space may be formed. However, it would be most difficult to make a connection between antegrade intimal space and retrograde subintimal space in this type. If this cannot be achieved, the usual reverse CART approach is performed, provided the antegrade wire has been advanced into the distal subintimal space.

3.3.4 Type 4: Both the Antegrade IVUS Catheter and the Retrograde Guidewire Are Located in the Intimal Space

The antegrade approach to penetrate the intimal lumen can be used when the antegrade guidewire seems to be present in the intimal space; however, shifting will be required depending on the site and timing of switching to reverse CART approach, because usually in such a case the antegrade wire cannot be operated thoroughly. Similar to Type 2, contemporary reverse CART approach can be tried by enlarging the subintimal space using a balloon with a relatively small diameter, such that the wire can be inserted into the true proximal lumen by retrogradely inserting a wire with high penetration ability and control such as GaiaNext2/3 towards the balloon intentionally during deflation of balloon. In many cases, by antegrade dilation of a large balloon, which is almost the same size as the blood vessel diameter, the wire can be guided into the obtained lumen, however, when there is a large distance between the antegrade retrograde wires, some inventiveness is required. For example, the balloon can be dilated as close as possible to the position of the wire, and the curve of the retrograde wire tip can be strengthened and penetrated towards the lumen dilated by the balloon. In this case, GaiaNext2/Next3 or Conquest Pro is often useful as a guidewire.

3.4 Conclusion

IVUS provides a lot of valuable information on CTO-PCI, in addition to information obtained from angiography. It seems possible to raise the initial success rate of the treatment by appropriately using IVUS in PCI for CTO with understanding specific IVUS findings in PCI for CTO and choosing appropriate wires to operate based on the theory.

4 Antegrade Wire Escalation and Parallel Wire

Makoto Sekiguchi

4.1 Introduction

Recently, there has been a great deal of progress in the development of the retrograde approach technique and the antegrade dissection reentry technique to perform percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) [1–4]. Especially, the retrograde approach technique is one of the valid strategies in CTO–PCI procedure. However, antegrade wire escalation and parallel wire are the simplest and most widely used CTO crossing techniques [5, 6].

4.2 Foundations of Antegrade Guidewire Crossing in All CTOs

Understanding both "intima" and "subintima" is important in learning the CTO–PCI procedure. In order, media and adventitia are present on the outside of CTO body, which occludes the coronary artery with intimal plaque. There is the external elastic lamina between the media and the adventitia. There is histologically weak connected tissue present in the media, especially near the external elastic lamina, which is called "subintima" (Fig. 4.1-a). A dissection in the subintima expands easily and widely in both longitudinal and transverse directions with movement of a guidewire tip and insertion of any device [7]. The resistance of subintimal tissue against the guidewire tip is much lower than that toward the intra plaque, so the guidewire seems to easily remain in the subintimal layer, making it hard to redirect the guidewire tip toward the intimal plaque. Arterial blood flow, guidewire handling, and insertion of a micro-catheter and an intravascular

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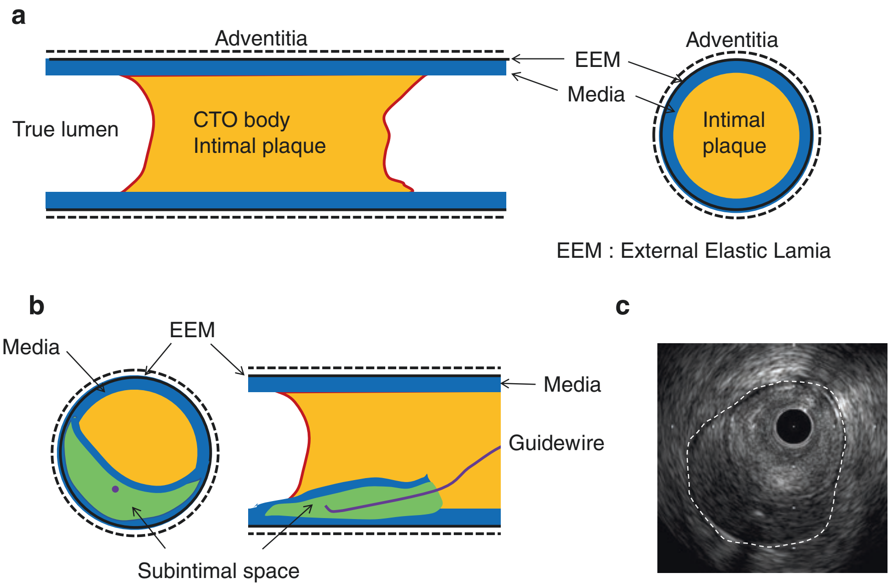


Fig. 4.1 "Intima" and "subintima" in CTO. (**a**) There are the media and the adventitia in order on the outside of CTO body which occludes the coronary artery with intimal plaque. There is the external elastic lamina between the media (EEM) and the adventitia. (**b**) Subintima is in the media, especially near the EEM. Once the guidewire enters into the subintimal space, the guidewire easily advaces into the subintimal space yet is difficult to cross to the distal true lumen. (**c**) The intravascular ultrasouds (IVUS) images shows the widely expanded subintimal space compared with cross-secctional image of b. Dotted circle indicates the EEM border. The subinatimal space is showed as the crescent-shaped are outside of the intimal plaque

ultrasound (IVUS) create a new space easily which is called "subintimal space." Once the subintimal space is spread widely, the adjoining intimal plaque is compressed, and redirecting a guidewire toward the intimal plaque becomes more challenging (Fig. 4.1 b and c).

Recently, a lot of prominent guidewires for CTO lesions have been approved. In general, as the tip stiffness of a guidewire becomes stronger, its flexibility becomes lower. Although a guidewire has better performance for CTO–PCI procedure, it is not able to demonstrate its ability without enough support and coaxial alignment. Guide catheters, which have >7 Fr and supportive shapes with bigger curves, should be used to provide enhanced supportability and visualization. Additionally, 7 Fr and 8 Fr guide catheters are available to perform the anchor balloon technique, the parallel wire technique, the IVUS-guided wiring, and the balloon trapping technique for exchanging over-the-wire (OTW) devices. Usage of a micro-catheter is mandatory. It provides better support and coaxial alignment and increases handling and penetrating ability of a guidewire in CTO lesion. Moreover, a micro-catheter allows guidewire tip reshaping without losing guidewire position and facilitates guidewire exchanges. In lesion with a side branch around the CTO entry, a dual lumen catheter (Twin-pass; Vascular Solutions, SASUKE; Asahi Intecc, Crusade; Kaneka) is used to direct the second guidewire into the CTO proximal cap. The system of the first guidewire in the side branch and the dual lumen catheter over its guidewire can provide better support and arrange the angle to the CTO proximal cap. The most important foundation of antegrade wiring is to continually ensure that a guidewire demonstrates its handling and penetrating ability; thus, a suitable guidewire, which is not unnecessarily stiff, is required for all the CTO–PCI procedures.

4.3 Antegrade Intimal Plaque Tracking Throughout CTO

The guidewire crossing technique only for a CTO lesion with antegrade approach fashion is divided between antegrade intimal plaque tracking throughout CTO and antegrade dissection reentry. Antegrade intimal plaque tracking throughout CTO means that a guidewire is passed from the CTO entry to CTO exit throughout the intimal plaque without tracking the subintimal space. Antegrade wire escalation and parallel wire are the most widely used in antegrade intimal plaque tracking throughout CTO. Contrastingly, antegrade dissection reentry means a guidewire in the subintimal space is navigated intentionally into the distal true lumen of the target coronary artery. The antegrade dissection reentry is categorized as a wire-based technique such as subintimal tracking and reentry (STAR), contrast-guided STAR, LAST (Mini-STAR), and device-based technique [8] (Fig. 4.2).

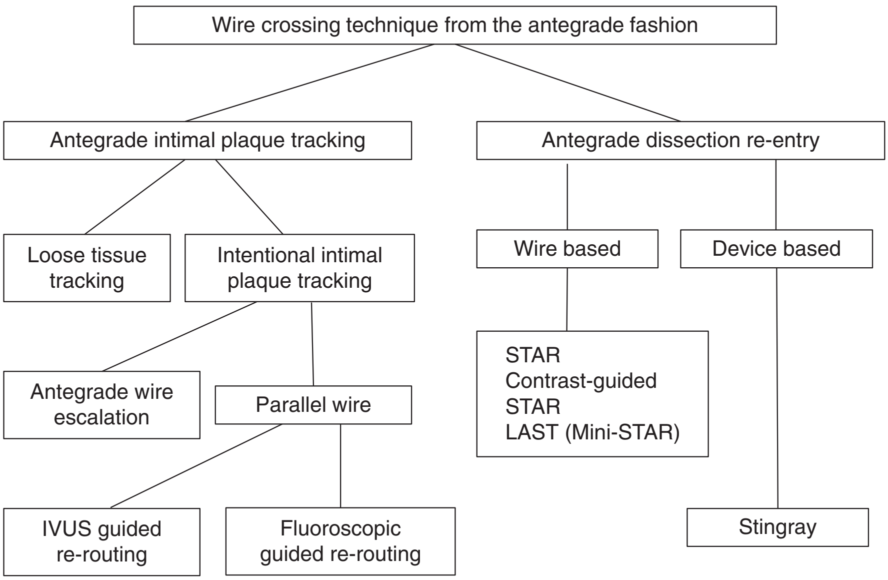


Fig. 4.2 Wire crossing technique from the antegrade fashion

4.4 Antegrade Wire Escalation

Antegrade wire escalation is one of the guidewire crossing techniques used to achieve the antegrade intimal plaque tracking throughout CTO with repeating guidewire exchange and reshaping the tip. Till date, these techniques constitute the foundation of all CTO–PCI techniques to accomplish a successful technique [6].

Guidewire Handling Techniques Guidewire handling techniques consist of loose tissue tracking, drilling, deflection control, and penetration technique in both antegrade and retrograde fashion. Loose tissue tracking is a guidewire handling technique used to navigate a guidewire with polymer-jacketed coat (Fielder FC, SION black; Asahi Intecc, PILOT 50; Abbott) through the loose tissue segment, which may be found in both short-duration CTO and old CTO. A guidewire with a tapered tip (XT-R, XT-A; Asahi Intecc, Whisper; Abbott) is usually used; the wire automatically advances into the loose tissue with only gentle rotation. Do not push the guidewire and dedicate to gentle rotation. Particularly, the loose tissue tracking technique seems to be effective for tapered shape and stump with CTO entry. Drilling, deflection control, and penetration technique are guidewire handling techniques used to achieve antegrade intentional intimal plaque tracking. The concept of antegrade intentional intimal plaque tracking involves intentionally advancing a guidewire throughout the intimal plaque, according to some aids. Some aids of guidewire navigation consist of expected vessel course from the angiogram, calcification and stents, which have been implanted, multi-slice computed tomogram (MSCT) information, tactile feedback, and IVUS findings. The drilling technique includes achieving the intentional intimal plaque tracking with controlled rotation of a guidewire in both directions. Usually, a guidewire with moderate tip stiffness (ULTIMATE Bross 3; Asahi Intecc, PROGRESS 40; Abbott) is used. The drilling technique seems to be effective for the remaining soft tissue of the CTO lesion when loose tissue tracking technique does not work. However, if there is a hard tissue in the CTO lesion, the guidewire easily turns away to the subintima and creates a large subintimal space. Deflection is a phenomenon in which the bending tip turns aside from a straight course against the resistance of occluded tissue when the guidewire is pushed into a CTO lesion. Deflection control technique is used to achieve the intentional intimal plaque tracking with repetition of deflection after the guidewire advance and turning the guidewire tip to favorable direction. This technique requires a guidewire that has good torque responsibility without whip motion, strong penetrating ability, and flexibility to track the expected vessel course. Usually, Gaia series and Gaia Next series (Gaia first, Gaia second, Gaia third, Gaia Next 1, Gaia Next 2, and Gaia Next 3; Asahi Intecc) are used. However, in CTO body, a space created by guidewire manipulation voids this concept, because guidewire requires the resistance to deflect even in the intimal plaque. Therefore, guidewire rotation should be minimum. CTO lesion with unknown vessel course is not suitable for a deflection control technique because of high complicated risk of a coronary perforation. The penetration technique consists of forward guidewire advancement into the very hard tissue such as a hard proximal cap, a calcified plaque in CTO body, and a hard exit. Usually, an extremely stiff guidewire (Confianza

Pro, Confianza Pro 12; Asahi Intecc) is used, such as a needle with clear visualization of the goal. To say nothing of penetrating manipulation, these guidewires easily make a coronary perforation during each use. The vessel course should be well understood. Guidewire step-down, which means to use softer tip guidewire, is sometimes effective after penetration of a hard tissue.

In each part of the CTO lesion, the guidewire handling technique is as follows.

CTO Entry The type of entry shape determines which technique should be applied to each CTO entry. At first, the loose tissue tracking technique should be attempted to tapered shape and stump with CTO entry. When loose tissue tracking technique is not effective or the entry shape of CTO lesion looks abrupt, a moderately stiff guidewire is rotated gently to look for a hollow (entry point) on the proximal cap. And then, while keeping the tip of guidewire at the hollow, the guidewire is rotated slowly on the hollow as an axis and is advanced into the proximal cap. When the hardness of the proximal cap obstructs the guidewire insertion, guidewire step-up should be performed. If there is a side branch adjacent to the CTO entry, the second guidewire can be manipulated effectively from the OTW lumen of a dual lumen catheter over the first guidewire in the side branch. When entry shape looks no stump or impossible to find a hollow with a guidewire tip, an IVUS examination over the guidewire in the side branch should be performed to find the occluded vessel and entry point. Then, the proximal cap is penetrated with a stiffer guidewire. If an IVUS catheter cannot be inserted into the side branch, MSCT information before CTO–PCI procedure should be applied.

CTO Body A guidewire is advanced through CTO body with some aids such as an expected vessel course from the angiogram, calcification and stents that have been implanted, MSCT information, tactile feedback, and IVUS findings. In the loose tissue tracking technique, the guidewire is only rotated. Do not push it the wire. If the guidewire cannot be advanced, the micro-catheter should be advanced closer to the guidewire tip to increase its supportability. The intentional intimal plaque tracking requires the operator to be always aware of guidewire tip movement. When it is difficult to manipulate the guidewire because of strong resistance, the micro-catheter should be advanced closer to the guidewire tip to increase handling ability of the guidewire or the guidewire should be exchanged for step-up (or step-down). When the guidewire loses the intimal plaque and enters the subintima, the manipulation of the guidewire should be stopped to prevent the development of the subintimal space. Confirmation of a point where the guidewire enters the subintima is needed to decide the next step. If possible, try rerouting the intimal plaque with the same guidewire from the proximal portion of its point. If this seems difficult, apply the parallel wire technique, retrograde approach method, or IVUS-guided rerouting.

CTO Exit When a guidewire tip reaches the distal true lumen throughout a CTO lesion, the antegrade escalation technique is successfully achieved. However, this is difficult to confirm only with tactile feedback. A system that is able to clearly visualize a CTO exit is required. The antegrade escalation and other antegrade wiring techniques without visualization of a CTO exit do not often succeed. Contralateral injection is mandatory to visualize CTO–PCI procedure well in most of the cases. Especially, selective injection in the collateral channel is more helpful.

4.5 Parallel Wire

The parallel wire technique is one of the most popular and fundamental techniques for CTO–PCI, although it has recently decreased in popularity because of the development of the retrograde approach method and the antegrade dissection reentry technique [6]. In the parallel wire technique (Fig. 4.3), when the first guidewire is advanced into the subintimal space, it is left in place, and a second guidewire is used to track the intimal plaque throughout CTO lesion [9]. Recently, a dual lumen catheter over the first guidewire is used to manipulate the second guidewire. Concerning the advantage of the parallel wire technique, the first guidewire, which acts as a marker, guides the intentional intimal tracking of the second guidewire. A combination of the first guidewire and dual lumen catheter increases the supportability of the second guidewire.

In the parallel wire technique, the second guidewire is required to be rerouted from a point where the first guidewire enters the subintimal space. Therefore, the

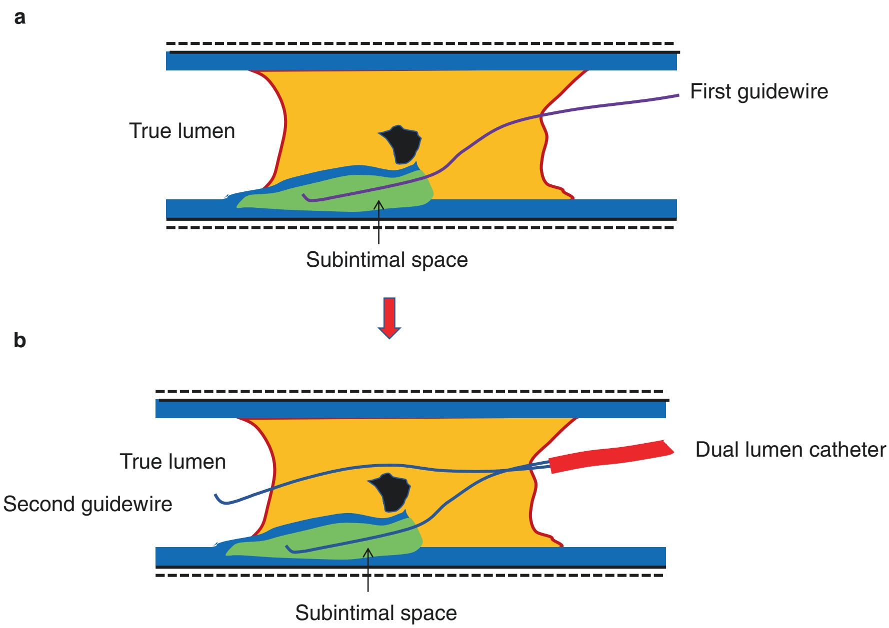


Fig. 4.3 Parallel wire technique. (**a**) The first guidewire is advanced into the subintima and is left in place. (**b**) The second guidewire with a dual lumen catheter is navigated into the distal true lumen

most important issue of the parallel wire technique is to confirm “rerouting point” where the first guidewire enters the subintimal space. When rerouting point is unclear, confirmation of the rerouting point with IVUS examination is required. In other words, usual parallel wire technique means fluoroscopic-guided rerouting with the second guidewire. And then, IVUS-guided rewiring using IVUS examination to confirm rerouting point required IVUS-guided rerouting with the second guidewire (Fig. 4.2). However, because insertion of an IVUS catheter over the first guidewire in the subintima might further expand the subintimal space, the IVUS-guided rerouting technique should not be performed in early phase of the antegrade intimal plaque tracking throughout CTO [10].

The parallel wire technique in each point where the first guidewire enters the subintima is as follows.

CTO Exit When the first guidewire enters the subintima around CTO exit, the parallel wire technique is recommended to start as soon as possible. Repetition of rerouting with the first guidewire might develop the subintimal space around CTO exit which compress the distal true lumen. Usually, the second guidewire is stiffer than the first one.

CTO Body When the first guidewire turns away with the hard tissue and enters the subintima, the second guidewire, stiffer than the first one, should be used as the second guidewire. When the first guidewire cannot follow the curved vessel course and enters the subintima, a guidewire more flexible than the first guidewire should be used as the second guidewire.

CTO Entry When rerouting point where the first guidewire enters the subintima is unclear and the length of CTO lesion is short, it might be helpful to start rerouting with the second guidewire from the proximal cap.

4.6 Optional Techniques of Antegrade Guidewire Crossing

Side Branch Technique In the antegrade intimal plaque tracking, the guidewire is often advanced into the distal true lumen of the side branch. Do not remove the guidewire in the true lumen of the side branch. A micro-catheter is advanced into the side branch over the first guidewire to exchange for a soft and safe guidewire. And then, a dual lumen catheter is advanced into the CTO body over its new guidewire, the antegrade intimal plaque tracking with the second guidewire is started through the OTW lumen. The system of the guidewire in the side branch and the dual lumen catheter can provide better supportability and guidewire handling ability (Fig. 4.4).

Balloon Trapping Technique In all CTO–PCI procedures, when a micro-catheter or any OTW device is removed or exchanged, the guidewire movement which can result in guidewire position loss, distal vessel injury, and artery perforation should

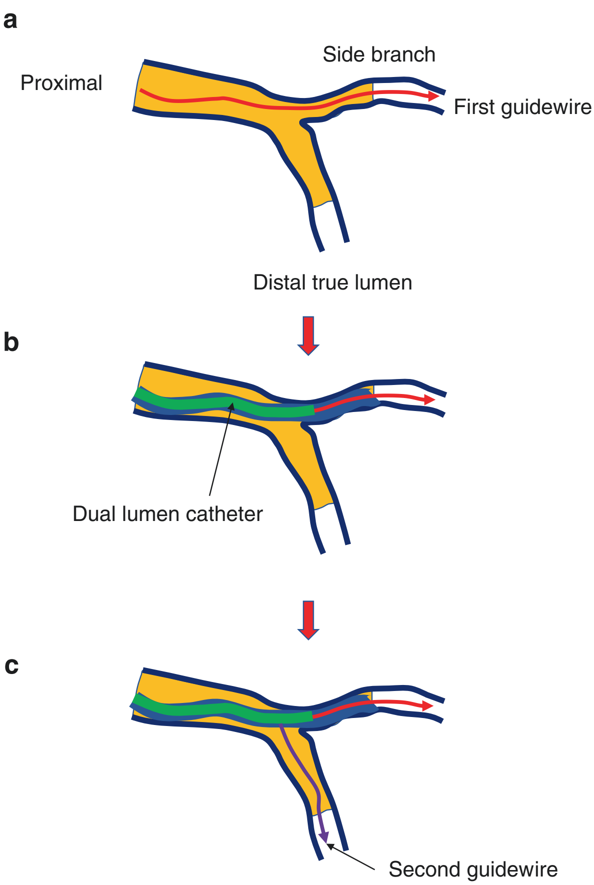


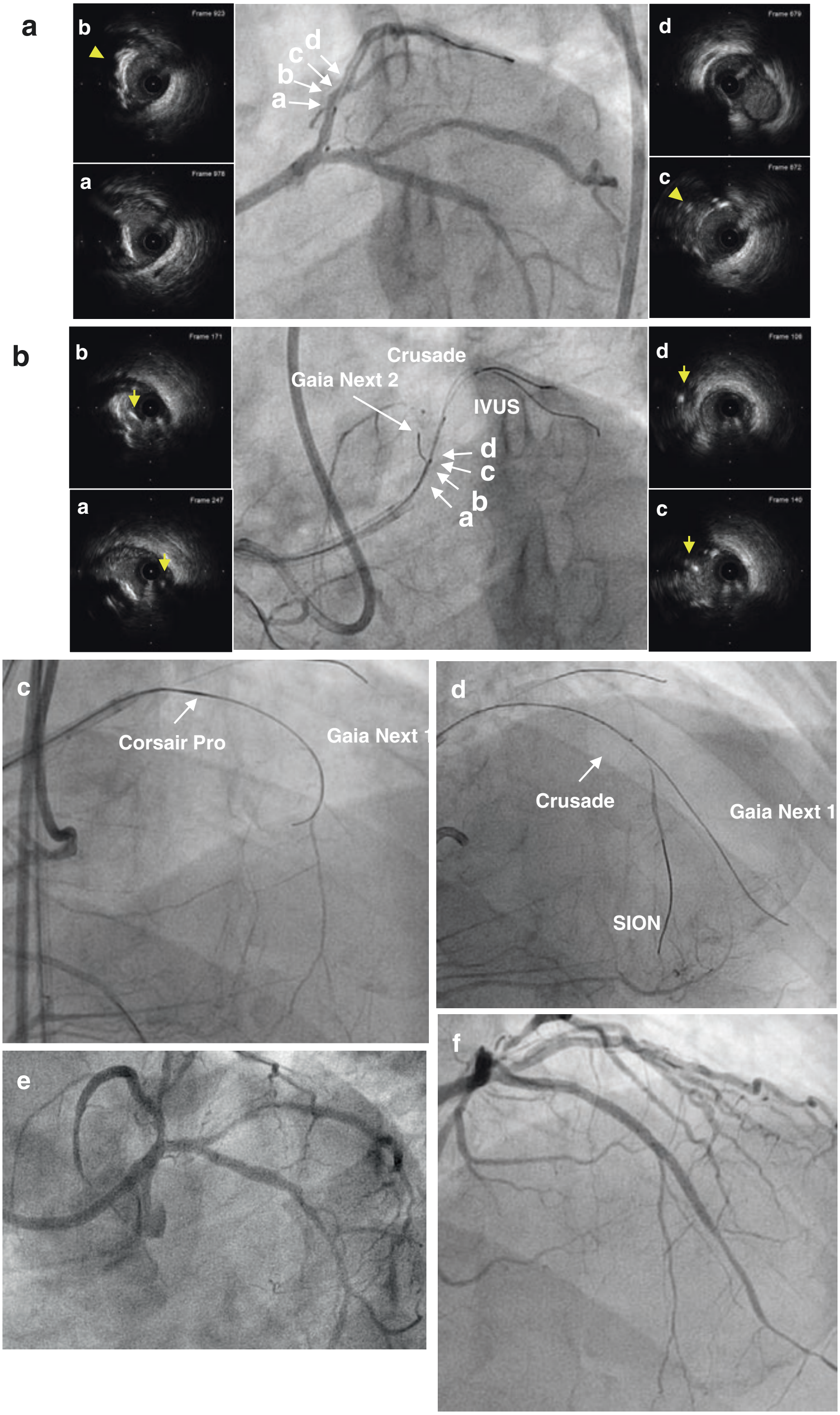
Fig. 4.4 Side branch technique. (**a**) The first guidewire is advanced into the side branch. (**b**) A dual lumen catheter is advanced over the first guidewire. (**c**) The second guidewire is navigated into the distal true lumen through the OTW lumen of the dual lumen catheter

be avoided. The balloon trapping technique is the most accurate and safest. A micro-catheter (or OTW device) is withdrawn into the guide catheter and the trapping balloon is inflated at the distal end. Further, the micro-catheter (or any OTW device) can be removed and exchanged accurately. However, this technique often entrains air into the guide catheter. Therefore, confirmation of back bleeding from the Y-connector is necessary to prevent coronary air embolization. A specialized balloon for the balloon trapping technique (KUSABI; Kaneka) allows the balloon trapping technique in a 6 Fr guide catheter.

4.7 Case Presentation

Case 1 The target lesion was a proximal left anterior descending (LAD) flush CTO with >20 mm long occlusion and the first diagonal branch at the entry. The proximal cap looked unclear according to the angiograms. A first-attempted procedure with the retrograde approach technique was failed by a local physician. An 8 Fr guide catheter, EBU4.0 (Medtronic) was positioned in the left coronary. A floppy guidewire and an IVUS probe (OptiCross; Boston) were inserted into the first diagonal branch. The IVUS findings showed the occluded LAD in 10 o'clock direction (Fig. 4.5-a, yellow triangle). Another guidewire was inserted into the first diagonal branch. A Gaia Next 2 guidewire through the OTW lumen of a Crusade dual lumen catheter was advanced into the CTO body with the penetration and deflection control techniques under IVUS guidance. The IVUS findings showed that Gaia Next 2 was in the intimal plaque at the CTO entry (Fig. 4.5-b, yellow arrow). The simultaneous usage of dual lumen support and IVUS guidance was very helpful in tracking the intimal plaque, such as flush proximal cap with a side branch. Then, the Crusade was exchanged for a Corsair Pro micro-catheter with the balloon trapping technique. The antegrade intimal tracking was tried to navigate the Gaia Next 2 with Corsair support into the distal true lumen of the LAD. However, the Gaia Next 2 was uncontrolled and was exchanged for a Gaia Next 1 guidewire (step-down). And then, the Gaia Next 1 was navigated into the distal septal branch (Fig. 4.5-c). Therefore, the side branch technique was applied. The Gaia Next 1 through the OTW lumen of the Crusade over a SION guidewire in the distal septal branch was successfully navigated into the distal true lumen of the LAD (Fig. 4.5-d). Finally, the CTO lesion was successfully revascularized with drug-eluting stents (Fig. 4.5-e and f). In this case, the penetration with dual lumen catheter support and IVUS guidance, antegrade wire escalation (step-down), the polite deflection control, and the side branch technique led a successful antegrade intentional intimal tracking throughout CTO.

Case 2 The target lesion was a posterolateral (PL) branch CTO with a large territory of the left ventricle. Four side branches of the PL were shown from good collaterals. In this lesion, these side branches were called the PL1, PL2, PL3, and PL4. An 8 Fr guide catheter VL4.0 (Mach1; Boston) was positioned in the left coronary artery. The shape of CTO entry was blunt (Fig. 4.6-a). A Crusade dual lumen catheter was advanced over a Runthrough NS guidewire (Terumo) in the obtuse marginal branch. An XT-R guidewire was navigated into the CTO body from the OTW lumen of the Crusade (Fig. 4.6-b). After exchanging the Crusade for a Corsair micro-catheter (Asahi Intecc) with the balloon trapping technique, the XT-R was advanced into the distal true lumen of the PL1 (Fig. 4.6-c). The Corsair was exchanged for the Crusade over the guidewire in the PL1. The XT-R through the OTW lumen of the Crusade was navigated into the PL2 with the side branch technique (Fig. 4.6-d). After 2.0 mm diameter balloon dilation (Fig. 4.6-e), the antegrade intentional intimal tracking was tried to navigate a Gaia first guidewire into the PL3 with the Crusade over the guidewire in the PL2. However, the Gaia first was advanced into the subintimal space of the PL4. An IVUS probe (Navifocus WR; Terumo) over the Gaia first was inserted to check the point of deviation to the subintimal space (Fig. 4.6-f). The parallel wire technique was performed after the confirmation of the rerouting point. The Crusade was advanced over the Gaia first in the subintimal space. Then, a Gaia second guidewire through the OTW lumen of the Crusade was navigated into the distal true lumen of the PL3 (Fig. 4.6-g). The side


a
b
a
d
c
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c
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b
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a
Crusade
Gaia Next 2
IVUS
d
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c
Corsair Pro
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SION
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Fig. 4.5 Case 1

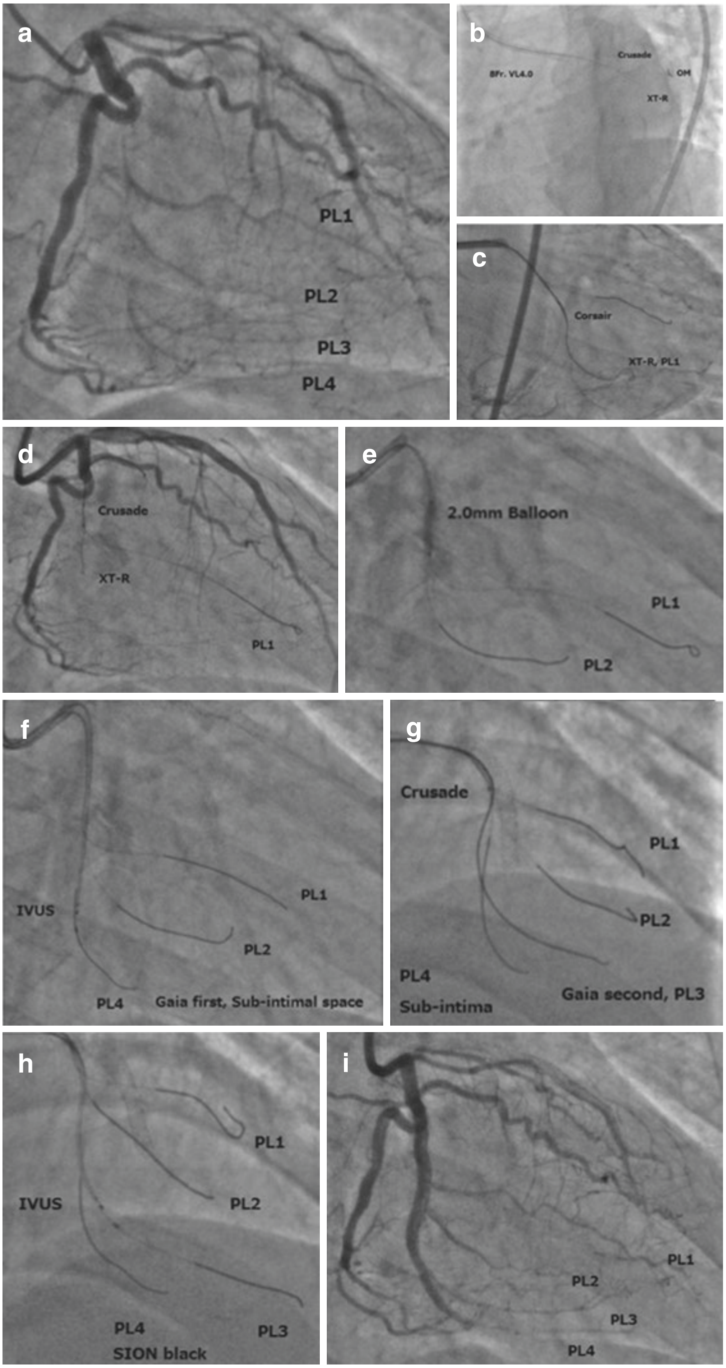
a
PL1
PL2
PL3
PL4
b
Crusade
8Fr. VL4.0
OM
XT-R
c
Corsair
XT-R, PL1
d
Crusade
XT-R
PL1
e
2.0mm Balloon
PL1
PL2
f
IVUS
PL1
PL2
PL4
Gaia first, Sub-intimal space
g
Crusade
PL1
PL2
PL4
Sub-intima
Gaia second, PL3
h
PL1
IVUS
PL2
PL4
PL3
SION black
i
PL1
PL2
PL3
PL4

Fig. 4.6 Case 2

branch technique was performed again. A SION black guidewire through the OTW lumen of the Crusade over the guidewire in the PL3 was navigated into the PL4 (Fig. 4.6-h). Finally, the CTO lesion was successfully revascularized without occlusion of any side branches (Fig. 4.6-i). In this case, revascularization of all branches seemed very difficult. However, the antegrade wire escalation, parallel wire, and side branch techniques were accurately repeated with every branch. The antegrade intimal plaque tracking throughout CTO was completely accomplished with step-by-step procedure.

4.8 Conclusion

The antegrade wire escalation and parallel wire are introduced as the antegrade intimal plaque tracking throughout CTO. To enhance the likelihood of successful CTO–PCI, the fundamental issues about the antegrade intimal plaque tracking throughout CTO are clear visualization of the CTO lesion and whole coronary arteries, applying various techniques to increase guidewire handling, and penetrating ability and accumulation of accurate procedures.

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5 Antegrade Dissection Reentry

Arun Kalyanasundaram

5.1 Background

Antegrade dissection reentry (ADR) with CrossBoss and Stingray (Boston Scientific, Maple Grove, MN, USA) has been a relatively new technique developed in the last several years. This as a strategy was subsequently incorporated into the hybrid algorithm when it was developed [1]. The approach can help achieve in the right setting—controlled and targeted reentry with good success rates [2]—and enables revascularization in certain patients that otherwise would not have had an option. In various registries, ADR has been utilized as the final revascularization strategy in about a quarter of the patients [2–4]. ADR, in the contemporary era, is not associated with markedly increase major adverse cardiac events (MACE) [5, 6]. Further, early studies [7–9] suggest that this strategy does not lead to adverse long-term outcomes. More recently, the Asia Pacific Chronic Total Occlusion Club (APCTO) algorithm [10] has also accepted ADR as a tool to facilitate reentry in certain anatomical situations.

5.2 CrossBoss and Stingray Devices

5.2.1 CrossBoss

The CrossBoss device has a 1 mm atraumatic tip (Fig. 5.1) and for practical purposes is a controlled elegant knuckle that can track in the vessel architecture utilizing the "Fast-Spin" technique [11]. Typically, it can be utilized as an initial strategy when the proximal cap is "tapered." Otherwise, initial penetration is performed with a penetrative wire and a microcatheter. This is followed by knuckling a wire such as

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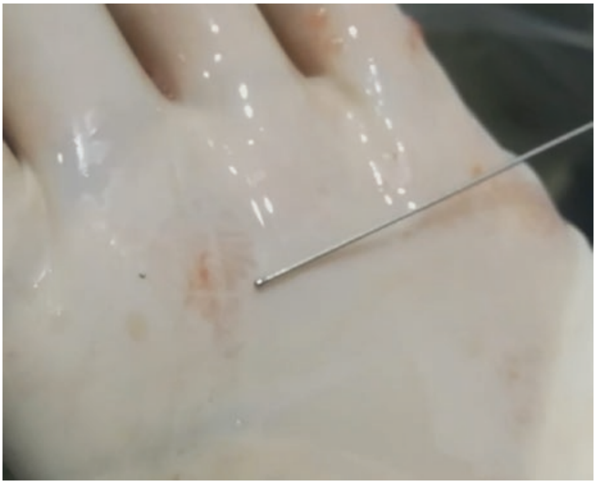

Fig. 5.1 Atraumatic tip of CrossBoss

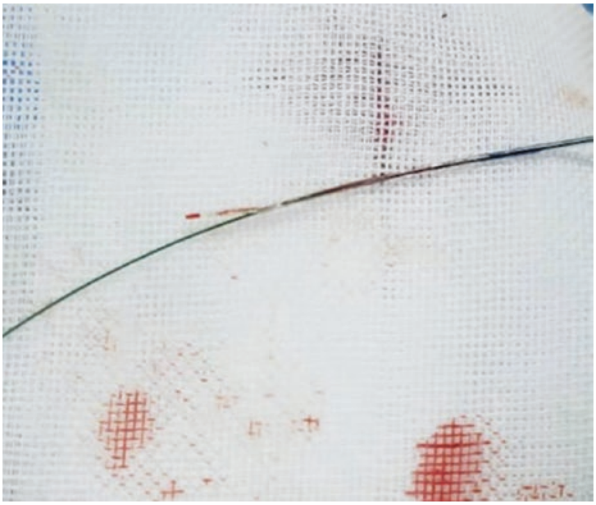

Fig. 5.2 Wire through sideport of Stingray balloon catheter

Fielder XT or Mongo wire (Asahi Intecc). A knuckle can be utilized safely in combination with CrossBoss. It is recommended that CrossBoss not be utilized with a penetrative wire since it will weaponize the penetrative wire, resulting in a possible perforation, in case the CrossBoss jumps forward.

5.2.2 Stingray Catheter

The Stingray catheter (Fig. 5.2) is a dedicated balloon catheter with the purpose of achieving targeted reentry at the landing zone. It is a flat balloon catheter with three ports. The proximal and mid port are 180° apart. When inflated the balloon lays itself in the subintimal space. One of the ports leads to the true lumen, and the other towards the adventitia. The Stingray balloon catheter when inflated layers itself in the subintimal space. This ensures that the ports of interest are 180° opposite to each other (then the balloon is inflated).

5.2.3 Stingray Wire

This is a dedicated reentry wire with a 12 g tip and a barb at the very end designed to penetrate from the subintimal space back into the true lumen.

5.2.4 Clinical Indications

ADR can be utilized in the following situations:

5.2.4.1 Primary Strategy

It can be utilized as a primary strategy when the probability of wiring the CTO efficiently and safely is low. The ideal scenario is where the proximal cap is discrete, there are no major side branches in the CTO body segment and at the distal cap, and the landing zone is relatively disease free. Again, there are solutions to problems if comes down to having to utilize ADR even in less than ideal situations. The proximal cap ambiguity can be resolved often by utilizing IVUS to determine the location of the cap. With more experience, operators can often achieve successful reentry even in diseased segments of the vessel. The problem of the branch at the distal cap has two potential solutions—reentry right at the cap and secure the other branch with a dual lumen catheter, or perform two separate sticks and then do a bifurcation stent strategy. It is critical that in these situations that operators utilize IVUS to confirm intraluminal position of the wire in both branches.

5.2.4.2 Secondary Strategy

ADR can be performed also when AWE fails as a strategy (secondary strategy). It is recommended that not multiple attempts at wiring be performed prior to using ADR as a bailout. The problem of utilizing multiple strategies or persistent wiring is enlarging hematoma which might reduce the chance of successful reentry.

In-stent restenosis (ISR) CTO is a special subgroup, and most hybrid operators have a low threshold for utilizing CrossBoss and the APCTO algorithm recommends to "consider CrossBoss" in this situation. Various factors need to be considered and can make CrossBoss more or less challenging to use:

- Stent expansion.
- Chronicity of the ISR.
- Length of the ISR.
- Proximal cap morphology (blunt versus tapered) and location (proximal to the stent versus inside the stented region),
- Location of the distal cap (inside the ISR versus distal to the stent).

Many times CrossBoss, as is often the case in non-stented regions, is utilized in combination with a knuckled wire.

A study in the UK [12] and subgroup analysis of a randomized trial in the USA [13] suggest that the use of CrossBoss results in a shorter CTO crossing time in ISR CTO.

5.2.5 Steps of ADR

1. *Get microcatheter/CrossBoss to the proximal cap*:

   This is done with a workhorse wire and a microcatheter/CrossBoss. The device can be reeled over the workhorse wire.
2. *Penetrate proximal cap:*

   If it is a blunt cap, it is recommended that penetration be performed utilizing a penetrative wire such as Gaia 3, Conquest Pro 12, Hornet 14 with a microcatheter. After this, the penetrative wire is exchanged for a knuckle wire.

   If a tapered cap, it might be reasonable to start with CrossBoss catheter directly.
3. *Crossing the CTO body:*

   After the knuckle gets going, the microcatheter can be exchanged to finish with the CrossBoss. During knuckling, it is important not to spin the wire but to only utilize linear motions till the "right" knuckle is formed. Crossing the CTO body itself can be done either by the CrossBoss catheter or by a knuckle—how it is crossed is immaterial. Many times a knuckle is utilized in conjunction with a CrossBoss catheter (Fig. 5.3).

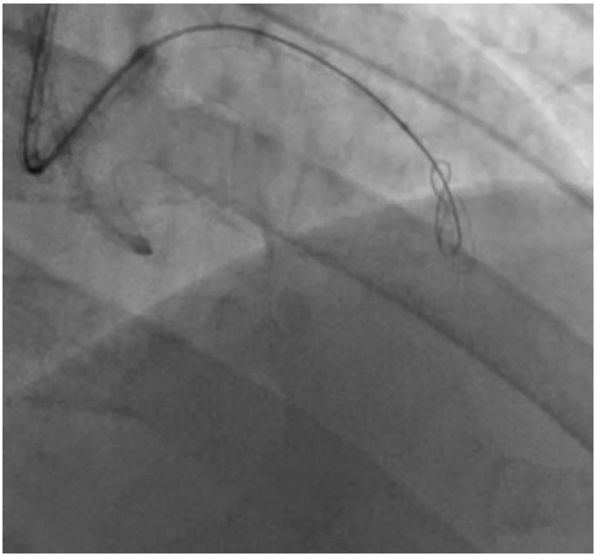

Fig. 5.3 Knuckle leading the CrossBoss catheter

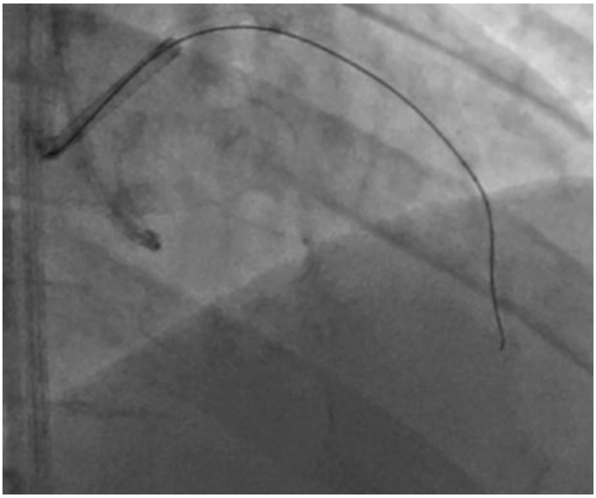

Fig. 5.4 Stingray balloon over the MiracleBros 12 wire

If a knuckle is utilized, it is generally recommended that a CrossBoss catheter be utilized to finish the last segment. This would enable a tighter space and facilitate reentry.

4. *Exchange the CrossBoss for the Stingray balloon catheter:*

   Once the CrossBoss catheter is in the reentry zone, it is exchanged for the Stingray balloon catheter over a stiff wire [stiff all the way to the tip such as MiracleBros 12 wire (Asahi Intecc)] (Fig. 5.4).

   In the situation of secondary strategy, the track created by the microcatheter (such as Corsair (Asahi Intecc, Nagoya, Aichi, Japan) or Turnpike (Vascular solutions, Minneapolis, Minnesota, USA)) is sufficient to deliver the Stingray balloon catheter directly to the reentry zone. Should there be difficulty in delivering the Stingray balloon to the landing zone, pre-dilation with a 1.5 balloon is sufficient to deliver the Stingray balloon.

5.2.6 Obtaining the Right View of the Stingray Balloon

It is important to obtain the correct view of the Stingray Balloon by moving the image intensifier until the right view is obtained. It is impossible to ascertain the "correct port" when the balloon is in the wrong view (Fig. 5.5a). The right view is basically a line and two dots (below) (Fig. 5.5b).

5.2.7 Reentry Utilizing the Stingray Balloon

Once the balloon is inflated, reentry is performed with the Stingray wire (Fig. 5.6a, b). Then the wire is removed, and often a "stick and swap" with a hydrophilic polymer jacketed wire such as the Pilot 200 is performed (Fig. 5.7a). It should be confirmed

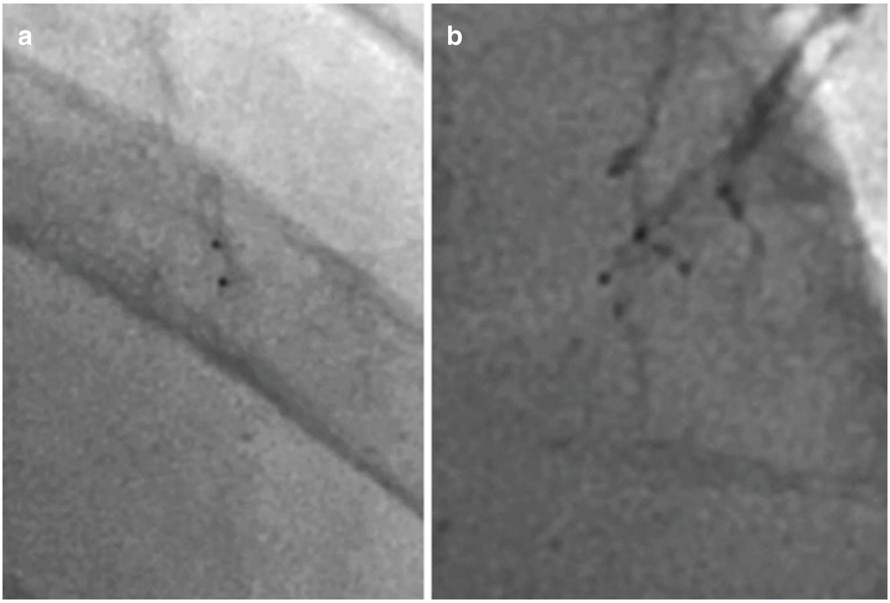

Fig. 5.5 (**a**) Wrong view of the Stingray balloon when the wings of the balloon are seen. (**b**) Right view of the Stingray balloon when the balloon is seen as one line and 2 dots with the vessel to the right of the balloon catheter

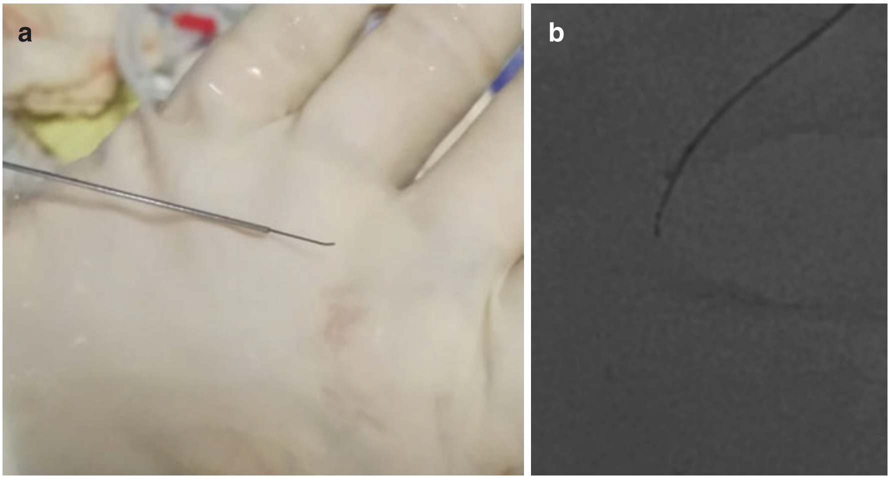

Fig. 5.6 (**a**) Stingray wire with preshaped tip. (**b**) Stingray wire through the proximal port of the Stingray balloon catheter making the "stick"

that the wire is in the true lumen by contralateral injection (Fig. 5.7b). This wire is then swapped out for a workhorse wire over a microcatheter (Fig. 5.8). Then the PCI is performed in the usual fashion. It important to note that during the PCI the procedure be done over the workhorse wire in order that there is no inadvertent distal wire perforation due to a CTO wire.

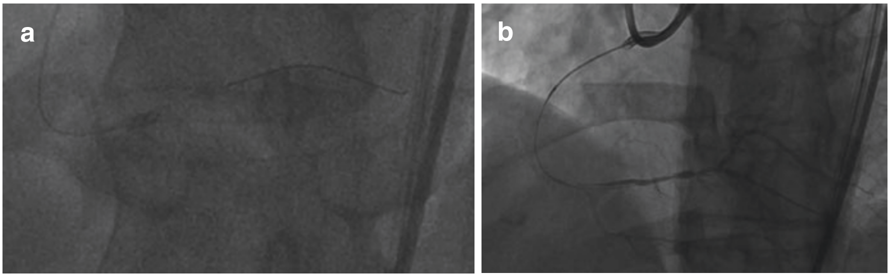

Fig. 5.7 (**a**) “Swap” performed with the Pilot 200 wire. (**b**) Confirmed that wire is in distal true lumen by contralateral injection

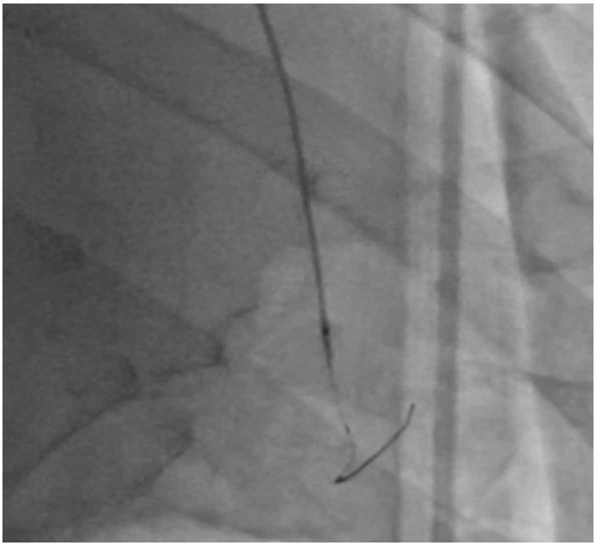

Fig. 5.8 Pilot 200 exchanged over the microcatheter for a workhorse wire

5.3 How to Utilize CrossBoss and Stingray

5.3.1 CrossBoss

CrossBoss is not a penetration catheter and is really designed to track the subintimal space rapidly. The torquer on the device is kept approximately 2–3 finger breaths from the introducer (Fig. 5.9). Also, it is primarily a spinning motion of the CrossBoss. It is important to often check the position of the CrossBoss to ensure that it is in the vessel of interest and not in a side branch. The device tends to travel straight and often hugs the outer curve of the vessel. Should CrossBoss be in a side branch, it can be redirected with a wire or with a knuckle (that is large enough to avoid the side branch). As already mentioned, it is recommended that CrossBoss be not utilized with a penetrative wire. As a safety measure in general, CrossBoss should either lead (especially towards the finishing segment) (Fig. 5.10a), or it should follow a knuckle (other than when wire redirect is being performed) (Fig. 5.10b).

Fig. 5.9 Distance of CrossBoss torque device from the Touey

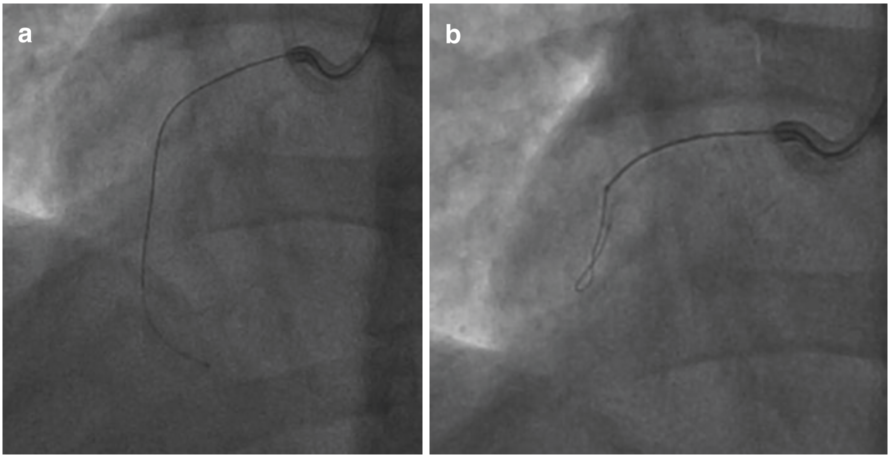

Fig. 5.10 (**a**) Finishing with the CrossBoss. (**b**) CrossBoss over the knuckle

5.3.2 How to Use Stingray?

5.3.2.1 Prep of the Balloon

The whole idea of the meticulous prep of the balloon is to ensure that it is visible. This is performed by obtaining a really good vacuum with a 20 mL syringe with a lock and a high-pressure stopcock (Fig. 5.11a). The suction with the syringe should be done at least twice. Then a small syringe (with a locking mechanism) with pure contrast (Fig. 5.11b) is utilized in order to ensure that the balloon is fully prepped

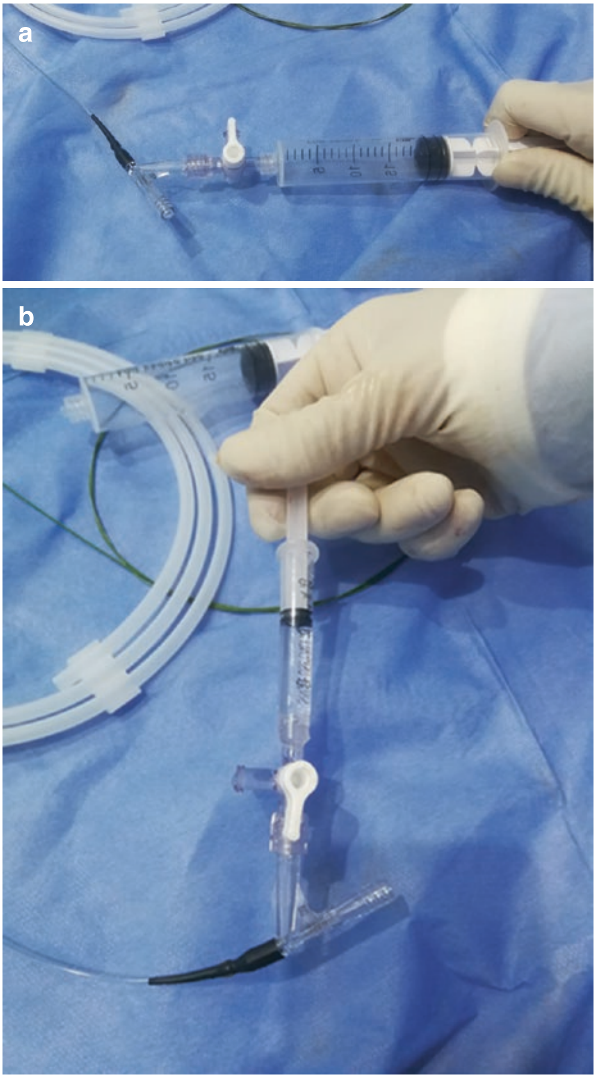

Fig. 5.11 (**a**) Suction performed with a 20 mL syringe twice. (**b**) Prep of Stingray balloon with 100% contrast in a 2–3 mL syringe with a luer lock

with contrast. Once the balloon is in the desired position in the landing zone, it is inflated to 4 atm. It is then important to move the image intensifier till the desired ideal position for reentry is obtained. To reiterate, tazhe wrong view (Fig. 5.5a) to reenter is when the face of the balloon is seen. It is important to see one line and two dots, i.e., the right view (Fig. 5.5b).

5.3.2.2 ADR When Using Knuckle Wiring

The hybrid algorithm suggests a primary ADR approach when the lesion length is >20 mm. APCTO algorithm does recommend knuckle wiring for "long plus"—CTO, i.e. prior wire failure, long lesion, ambiguous course, tortuous course, and excessive calcification. It is important not knuckle past the distal cap since this would make reentry difficult. The CrossBoss is often utilized to "finish" the subintimal tracking. This ensures a "tighter" subintimal space thereby improving the chances of reentry.

5.3.2.3 Choosing a Reentry Zone

Ideally, the reentry zone or the landing zone should be right beyond the distal cap. A relatively disease free area can be chosen especially when operator experience with ADR is limited. Multiple factors affect the suitability of a reentry zone—Calcification, plaque load, lumen size, distance of first wire to true lumen, hematoma size, stability of Stingray balloon, and operator experience. Finally, it is important not to be dogmatic about the reentry zone. If the initial area does not work, it is important to move to a new reentry zone.

5.3.2.4 Stingray Balloon to the Reentry Zone

Stingray balloon catheter is advanced over a wire stiff all the way to the tip such as the MiracleBros 12 wire (Asahi Intecc).

5.3.2.5 Reentry Through the Stingray Balloon

Then the Miracle wire is removed and the Stingray wire is advanced through the balloon catheter and a "stick" is performed. It is important to do this without just trying to wire the port, but to actually stick the port. Then after the stick, the Stingray wire is removed and then the polymer jacketed wire (often the "Pilot 200" is utilized to reenter the track into the true lumen again.

5.4 Tips and Tricks with ADR

5.4.1 Adequate Backup

Success in ADR is really dependent on good guide support. Larger guide size, preferably at least 7 Fr, along with improved guide support techniques is critical. Often, Amplatz guides for the RCA and extra backup guides for the left system are utilized. Other techniques such as guide extension catheters and anchor balloon are sometimes needed for good backup.

5.4.2 Switch Early to ADR

Should antegrade wire fail, switch early to ADR. Multiple attempts at wiring often result in large subintimal space and make reentry extremely challenging.

5.4.3 Control of Inflow

Controlling the inflow of blood into the CTO vessel can minimize hematoma formation and improve the success of Stingray. A large hematoma is probably the biggest reason ADR fails.

1. Removal of the antegrade contrast syringe is highly recommended after the wire has entered the subintimal space. This would avoid inadvertent injection of contrast into the subintimal space, which might enlarge the hematoma and reduce the chance of successful reentry.
2. It might also be reasonable to utilize a Trapliner (Vascular Solutions, USA) in the antegrade guide in order to reduce inflow into the antegrade guide.
3. Routine Subintimal TRAnscatheter Withdrawal (STRAW) [14] through the Stingray balloon catheter is recommended since that would reduce the hematoma. Variations of STRAW such as through a microcatheter adjacent to the Stingray balloon or even through the microcatheter prior to insertion of the Stingray balloon can be performed. This is done by attaching an empty indeflator to the end of the Stingray balloon or the microcatheter, when the wire is removed to exchange for the Stingray wire, and kept negative for a couple of minutes, while the correct view for reentry is ascertained. Aspiration could also be performed by a 20 mL syringe (Fig. 5.12).

   It is important to use syringes with a lock since only this will help achieve adequate vacuum.

Fig. 5.12 STRAW performed through a 20 mL syringe with a luer lock

5.4.4 Routine Stick and Swap

Routine use of the "stick and swap" technique is recommended. The Stingray wire has high penetration force and may result in distal vessel dissection if used to wire a distal true lumen, especially in diseased vessels. In general, a polymer jacketed wire with adequate penetrative force is utilized for this purpose [often times Pilot 200 (Abbott) is utilized].

5.5 Problem Solving in ADR

5.5.1 Proximal Cap Challenges

5.5.1.1 Impenetrable Proximal Cap

All the modalities to increase backup should be first line before more aggressive maneuvers.

5.5.1.2 Balloon Assisted Subintimal Entry (BASE)

This works by inflating a 1-to-1 sized non-compliant balloon. The microcatheter wedged against the balloon and a hydrophobic polymer jacketed wired into the subintimal space (and knuckled) (Fig. 5.13). This works particularly well when the part of the vessel proximal to the proximal vessel is diseased since it makes it much easier to dissect the vessel.

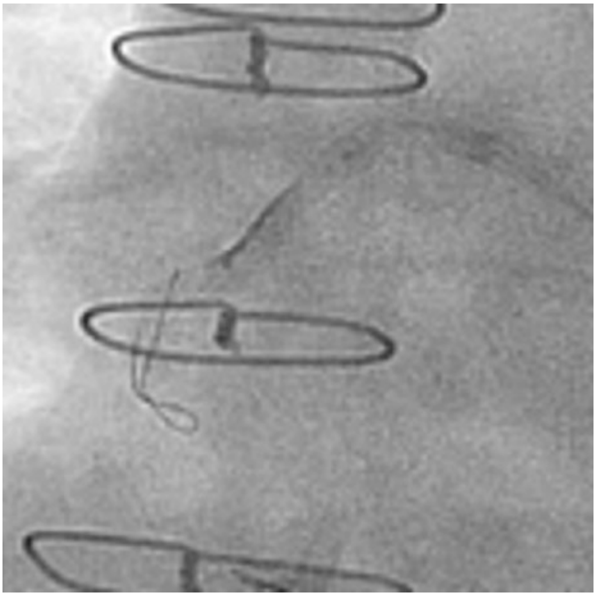

Fig. 5.13 Microcatheter wedged against vessel wall with a 1-to-1 balloon, and then a knuckled wire advanced through the microcatheter into the vessel wall

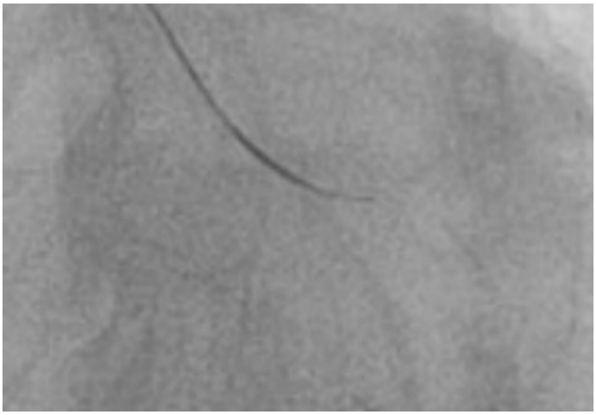

Fig. 5.14 Vessel wall entered with penetrative wire

5.5.1.3 Scratch and Go

In scratch and go, a still penetrative wire is used to penetrate into the vessel wall and a microcatheter is wedged into the vessel wall (Fig. 5.14).

Subsequently, a knuckle wire is advanced into the subintimal space.

There are other options such as application of laser at the proximal cap, or going retrograde and utilizing a knuckle to soften the proximal cap.

5.5.2 Crossing the CTO Segment

Whether it is a knuckle or CrossBoss to cross the CTO segment is immaterial. It is recommended that if a knuckle is utilized in crossing the CTO segment, that a CrossBoss be utilized to finish up to the landing zone. The CrossBoss tends to travel straight and many times can end up in a side branch. So it is important to check frequently with multiple projections that the device is in the vessel of interest and not in a side branch. Should it end up in a side branch, a wire redirect or a knuckle redirect can be performed, and then the CrossBoss can track over the wire/knuckle. A polymer jacketed wire such as the Pilot 200 is utilized for this purpose often (wire redirect), and a knuckle wire can be performed with one of the wires to avoid the side branch.

5.5.3 Reentry Challenges

It has already been discussed that "stick and swap" be the preferred strategy to reenter into the true lumen. Subintimal TRAnscatheter Withdrawal (STRAW) [14] of hematomas compressing the distal true lumen was introduced a few years ago. "Routine STRAW" should be performed over the Stingray balloon catheter. It is also important to remember to not be dogmatic about the reentry zone. Just like sometimes it is important to move where Reverse CART is performed, Stingray reentry zone might sometimes be needed to done more distally or proximally. Also, it is important to try and utilized another penetration wire such as the Gaia 3rd, Gaia next 3rd, Conquest 12, or 8/20 (Asahi Intecc), Hornet 14 (Boston scientific) for this purpose. Also, it is generally recommended that multiple sticks be done with the penetration wire. Such an approach often results in a fenestration and then subsequently the swap can be performed more easily.

When STRAW technique has not helped resolve the issue of filling a "double-blind stick-and-swap" [15] can be undertaken to address the problem of lack of visualization of the landing zone or target vessel.

Finally, the "double Stingray technique" to deal with bifurcation at the distal cap [16] has further increased the applicability and success of antegrade dissection reentry as a strategy. This approach can be undertaken when antegrade wire escalation has failed, and there is no viable retrograde option (or has failed).

5.6 Conclusions

ADR is an important component of the current CTO algorithm globally in the present day and age. It is important to limit the dissection length and obtain reentry as close to the distal cap as feasible. Also it is important to realize that the device based reentry is completely different than wire based techniques such as LAST and STAR given that this can be done with much more incredible precision and consistency.

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6 How to Read and Find the Appropriate Collateral Channel for the Retrograde Approach

Gerald S. Werner

6.1 Summary

Recent developments in the technical approach, both in strategy as well as available tools, have led to a greatly improved success rate for the recanalization of a chronic total coronary occlusion (CTO) which is now beyond 90% in experienced hands [1]. One of the major developments contributing to this success is the introduction and development of the retrograde approach accessing the distal vascular bed of an occluded vessel via collateral pathways [2]. The following chapter will focus on the anatomy and function of collaterals and their proper assessment by angiography, which are important criteria for the selection of the appropriate channel for a retrograde approach.

6.2 Anatomy of Collateral Connections

The fact that collaterals exist between occluded and open coronary segments was detected as early as 400 years ago. Ensuing was a century long debate among anatomists whether these collateral connections were pre-existent or developed anew in case of an occlusion. That debate was finally concluded by studies conducted by Baroldi and the Scot anatomist Fulton in the middle of the last century [3]. The in vivo study of the collateral anatomy then became possible with the introduction of coronary angiography. In 1974 Levin published an extensive analysis of the variation of collateral connections in the territories of occluded coronary arteries [4].

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His category of 22 individual pathways is still valid and a valuable source of information and can help to categorize possible interventional collaterals also for the retrograde approach [5].

Most importantly it needs to be realized that collateral pathways do coexist, and rarely do we find only one predominant connection. Even in that latter case, other pathways may be found by exploration with a wire as they may be dormant due to the fact that collateral supply will always pass via the ones with the lowest resistance [6]. For example, we may have a large collateral connection from the apical LAD to the RCA, but still we will find septal connections which are not active because of their higher resistance [7].

The predominant site of a CTO is the right coronary artery (RCA). Levin described ten predominant pathways, six of them originating from the left coronary artery (LCA) and four were ipsilateral pathways. The contralateral supply from the left anterior descending artery (LAD) can either run through the septum, which is the preferred interventional route, or via the apex, which is also often accessible for the retrograde approach. In addition, there may be connections via a LAD and acute marginal of the RCA connection which in practice often enters the occlusion close to the distal cap and therefore is not ideal for a retrograde access. The connections from the left circumflex artery (LCX) run through the atrioventricular groove and show varying degrees of tortuosity, making them viable retrograde options. More distal connections from the LCX run via epipericardial connections from an obtuse marginal (OM) to the distal posterolateral (PL) branch of the RCA. A rather rare connection is between the atrial branch and a proximal conus branch of the RCA. The ipsilateral connections are more difficult to utilize for a retrograde approach as they are of various tortuosity, but they may present an interventional option [8]. The Kugel's collateral connects a conus branch with the PL system, while there are connections from OMs to the distal RCA either directly to the distal bed or to another OM distal to the occlusion. Again, like in connections from the LAD to an OM, the collateralized OM often inserts close to the distal cap and therefore does not provide the angle towards the distal cap. In addition, we may find more exotic pathways running from a conus branch cranial around the heart to insert in to the distal PL system not observed in Levin's study.

In the recent application of Levin's approach to describing collateral pathways McEntegart et al. even described 20 collateral patterns in RCA CTOs, with the predominant supply via the septum in 72% of cases, the atrial connection in half of all cases followed by ipsilateral bridges, the apical LAD to RCA connection, LAD branches to OMs and the Kugel's collateral.

The second most frequent CTO is located in the left anterior descending artery (LAD). Levin observed seven major connections, four from the RCA, two ipsilateral as epicardial connections from a diagonal or obtuse marginal branch, and one ipsilateral between septal branches of the LAD proximal and distal to the occlusion. The RAO connections mirror the connections in case of a RCA CTO. The supply might run via the septum from the PDA, or from acute marginal branches from the RCA or via a proximal conus branch, and finally via the apex. In addition, in left dominant circulations there could a septal connection from the PDA originating from the LCX to the occluded LAD [4]. Interestingly, the frequency distribution observed by Levin with rare septal and more frequent epicardial connections does not reflect the daily practice, where the group of McEntegart described 13 distinct patterns [5]. They observed septal connections from the PDA to the LAD in half of all patients, then followed by the acute marginal to LAD and ipsilateral OM or diagonal to LAD pathways in about 20–25% each. Conus branch connections from the RCA were observed in 18%, septo-septal connections in 16%.

Whether these connections are accessible for an interventional approach again is determined by their tortuosity, distensibility, and the insertion point relative to the distal cap of the occlusive lesion.

The LCX is the least frequent CTO, and it is often the most difficult one to treat, which leads to the inclusion of the LCX as an adverse factor in the prediction of a successful recanalization by the PROGRESS score [9]. Levin observed five distinctly different pathways for a LCX CTO [4]. He found an ipsilateral connection via atrial branches as the most frequent, followed by ipsilateral OM connections or from the diagonal system. The RCA may supply the distal bed via atrial connections through the atrioventricular groove or distal OM branches. Also McEntegart et al. observed a less frequent number of coexisting collaterals for a LCX CTO [5]. The patterns are very much dependent whether the coronary circulation is left or right dominant. They categorized 12 different patterns of connections, the most frequent being diagonal to OM in about 30%, and connections from the RCA through the AV groove in 20–30% depending on the dominance, other connections are observed in the range of 10% or less.

For the sake of the interventional approach, the basic division is between septal, atrial, and epicardial connections (Table 6.1). The majority of connections for RCA and LAD CTOs are septal connections. These pathways run through the myocardium of the interventricular septum, but especially the basal connections of the first septal sometimes connect running across the right atrium and enter the distal RCA bed either separately through an intermediate branch at the crux cordis or into the proximal side branch of the PLA of the RCA. This is just one example that the rules about the anatomic course and distinctions between septal and epicardial pathways can vary individually. The general idea that septal pathways are less prone to severe complications when damaged during an interventional attempt to pass them as opposed to the more fragile epicardial connections should always be taken with caution, and the primary rule must be to avoid damaging collaterals.

It must be kept in mind that collaterals from septal origin may then pass towards the epicardium and vice versa. This is most evident in connections from the septal

Table 6.1 Collateral pathways and their interventional suitability

	Corkscrew-like morphology	Length of access route	Applicability	Distensibility
Epicardial	Various	Long	Moderate	Not dilatable
Atrial	Often	Medium	Moderate	Not dilatable
Septal	Slight	Short	High	Dilatable

branches of the LAD to the acute marginal branches of the RCA. Another example are branches which originate from the first septal and then turn towards the base of the heart and run across the right atrium before entering the RCA either very proximal in the PL branch or as a separate small intermediate branch. Damage to these connections will not be "protected" by the muscular septum but may create severe complications by intramural hematoma expansion and compression of cardiac cavities.

6.3 Angiographic Visualization and Assessment of Collateral Connections

The first and most important step when considering the retrograde approach is the angiographic visualization of the collateral pathways. For a perfect visualization it is important to avoid panning during filming, and to allow enough time for the contrast medium to reach the occluded segment. Contrast should be forcefully injected, and a large diameter catheter is helpful to reveal the smaller collaterals. The frame rate for the cineangiography should be increased (e.g., 15/s) to improve the detection of even tiny connections.

As the majority of CTOs are located in the right coronary artery (RCA), the main source of collateral supply runs through the septum, and these are the most frequently used interventional pathways. These septal channels can be best viewed in their entire course from a plain 30° right angle, with additional information on the entry into the channel provided from a cranial angulation, and the exit into the posterior descending artery (PDA) from a caudal angulation. Likewise, the connection from a RCA donor artery to an occluded left anterior descending artery (LAD) can be viewed. Other connections via the atrial grove between the left circumflex artery (LCX) and the RCA can be visualized both from the right and left anterior oblique projections at best with a caudal angulation. However, the takeoff of these channels may vary considerably and needs individually adjusted gantry angles.

Among the important features for the angiographic assessment of a possible suitable route for wire access to the distal occluded segment is the diameter of the collateral connection. This was initially graded in 3 categories of collateral connection size (CC) (CC0: no angiographic continuous connection; CC1: threadlike connection (<0.4 mm); CC2: side branch like connection (>0.4 mm)) [10]. There are also occasional large connections, especially via the apex of >1 mm diameter which could be labelled CC3 connections. Other important features to consider are the tortuosity of the connection and the angle of takeoff from the donor segment, as well as at the site of entry into the receiving segment. The length of the connection can be of relevance as the length of the interventional catheters is limited.

The tortuosity of a collateral can be of various relevance, as some bends will be straightened when a wire is advanced, some bends may be less distensible and then cause an increasing resistance to the advancement of the wire and microcatheter (Fig. 6.1). Therefore, the sheer fact of a tortuous connection alone should not determine the utility as an interventional pathway. Osamo Katoh in his first presentations on the retrograde transcollateral approach had used a ratio of amplitude and

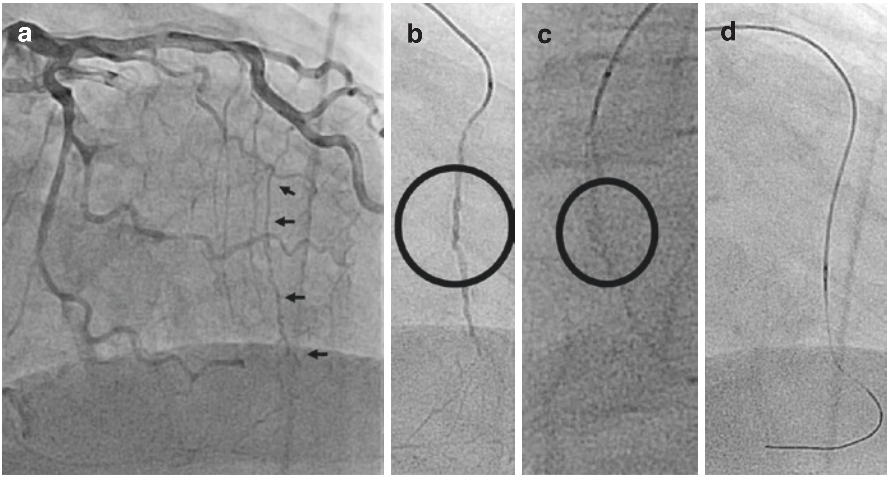

Fig. 6.1 (**a**) Several septal pathways are visible on this RAO 30° view. The one marked by arrows was selected for the interventional access. (**b**) However, the attempted wire passage with a Sion (ASAHI Intecc) stopped in the middle of the vessel. Selective injection did not reveal the cause on the RAO view (circle), but the LAO view (**c**) showed a severe tortuosity with a more than 180° reverse bend (circle). (**d**) Realizing this obstacle, the wire could be manipulated through this bend with a 90° tip angle

collateral diameter as a measure to determine the collateral suitability. A value of >2 would describe moderately tortuous connections, a value <2 would define severe tortuosity.

From their detailed analysis of collateral angiographies with a view to their interventional suitability McEntegart et al. suggested a collateral scoring system. This score is rather detailed and complex, and it has not yet been validated in a larger independent series. A much simpler score was suggested by Huang et al. limiting it to the collateral connection size and the tortuosity as the major determinants of success to pass the collateral by a wire [11]. The definition used by this group to define high tortuosity is the observation of high-frequency curves, that is, a curve of more than 180° when the vessel diameter is less than 3 times the size of the curve. If in epicardial connections two or more of these high-frequency curves are observed within a 2 mm distance this epicardial is considered tortuous. Regarding the septal connections, some of these bends will straighten themselves through the cardiac cycle. If more than one such bend stays unaffected by the cardiac cycle, it is considered as a tortuous septal.

The issue with validating these kinds of scores is the fact that passing collaterals with a wire requires above all a long experience and familiarity with these dedicated wires, which continue to receive further innovation and refinement. A difficult anatomy may pose an obstacle to less experienced operators, which can be overcome by others. Therefore, all scores can serve as a general guide especially for the novice, but they cannot replace the trial in case certain unfavourable collaterals may be the only option for a successful interventional treatment.

6.4 Time Variation of Angiographic Visualization of Collateral Connections

The assessment also has to take into account that several collateral pathways may coexist, and that their appearance may change depending on the haemodynamic status of the collateral donor artery (Fig. 6.2). Therefore, any previous angiograms should be carefully analysed. Disappearance of a collateral connection between two angiograms at different time points may not signify the actual closure of the collateral connection, but rather that it is functionally dormant. It is suggested by some operators to use a low-pressure balloon occlusion of one of the pathways to explore alternative routes, which are more likely accessible to a wire passage. A common practice is the selective injection into channels to identify by this direct contrast application possible distal run-off into the distal coronary bed of the occluded artery (Fig. 6.3).

Careful wire probing may still achieve wire passage even when connections are not clearly visible, especially in septal pathways. This is the basis of the so-called septal surfing approach to pass from the LAD towards the distal bed of an occluded RCA and vice versa [12].

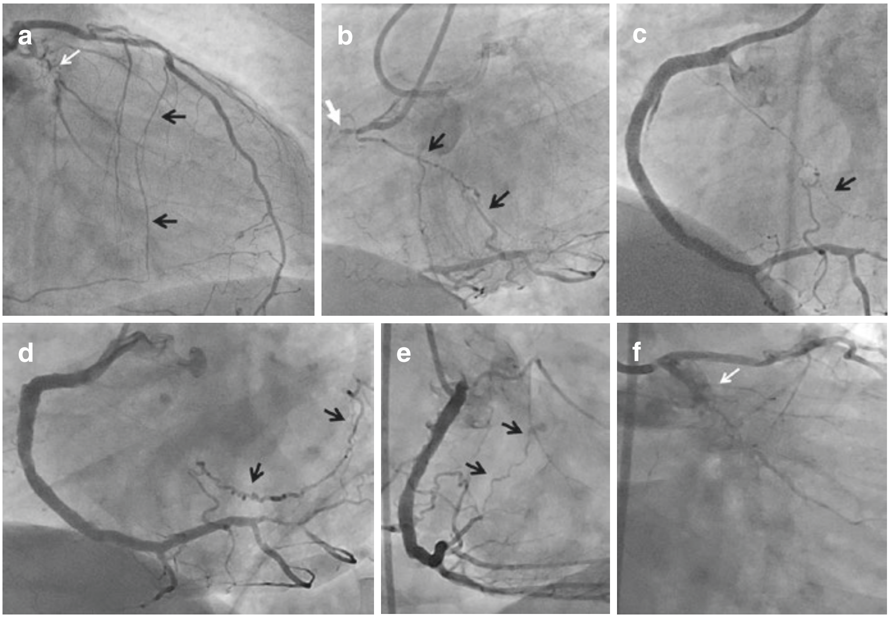

Fig. 6.2 (**a**) A patient with three-vessel disease and a circumflex occlusion (white arrow) with bridging collaterals. There are septal connections to the occluded right coronary artery (black arrows). (**b**) The occluded right coronary artery (white arrow) receives also ipsilateral collateral supply via a Kugel's artery (black arrows). (**c**) After staged recanalization of the right coronary artery a thin connection becomes already visible (arrow). (**d**, **e**) Four months later at the time of the planned circumflex recanalization, this connection is developed into the main supply for the distal left circumflex artery (arrows). (**f**) The bridging collaterals are no longer the major source of supply for the occluded circumflex (white arrow)

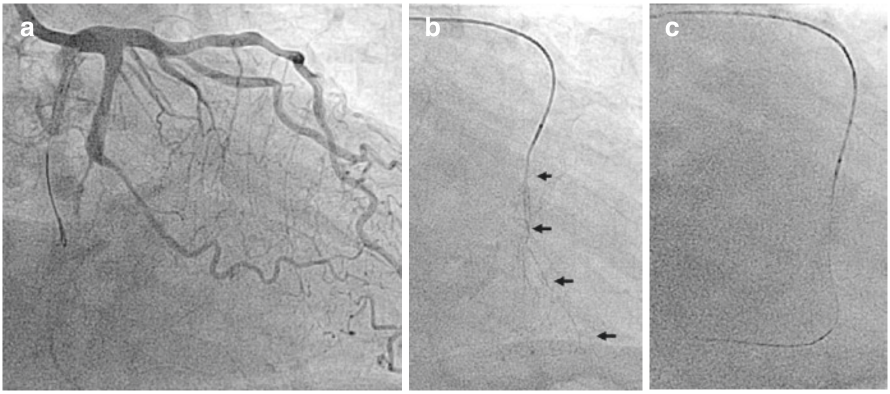

Fig. 6.3 (**a**) A left circumflex occlusion with ipsilateral filling of the distal PDA, but no clear collateral pathway. (**b**) Selective injection reveals a faint CC1 connections turning towards the PDA (arrows). (**c**) This could be passed by a Sion wire (ASAHI Intecc), but the distal turn of the wire looks like it took an invisible channel inward of the one visualized in (**b**)

6.5 Can We Augment Collateral Visualization?

Collateral filling by contrast medium is dependent on the pressure gradient across the collateral and its diameter. To improve the collateral visualization, we would ideally increase the collateral flow. In analogy to the epicardial coronary artery, however, collaterals do not typically have a smooth cell layer that would respond to vasodilators as nitroglycerin [13]. Collaterals do respond to shear stress as a principle of their recruitment from the initial arteriolar connection to a fully functional collateral, but this is not instantaneously affected [14]. Therefore nitrogylcerin will not enlarge the diameter of the collateral, but it may still improve their identification by increasing flow in the receiving vessel.

Furthermore, there is an obvious rule that there cannot be normal regional myocardial function without blood supply. Therefore, if a normally contracting area distal to a coronary occlusion must receive sufficient collateral supply to uphold the viability. If on a routine diagnostic angiogram, no such supply is observed there must be different sources present which were not yet detected. A typical case is a LAD occlusion supplied by a conus branch from the RCA that originates separate from the RCA ostium. These separate branches need to be searched for and sometimes provide even an interventional pathway.

6.6 The Functional Capacity of Collaterals

A detailed discussion of the collateral circulation relevant to coronary artery disease can be found in many reviews [13, 15, 16]. Collaterals develop through arteriogenesis, that is, through the recruitment of preformed and pre-existing inter-arterial connections mainly driven by shear forces along the pressure gradient that develops when the native vessel is occluded [14]. Some of these connections may be pre-existent to such an extent that they are immediately recruitable in case of a vessel occlusion, as shown during balloon occlusion in non-diseased coronary arteries [17]. The functional assessment of collaterals has revealed that in patients without well-developed pre-existing collateral connections, collaterals required between 2 and 12 weeks to fully develop their functional capacity [7].

The physiological assessment of collateral function is best done with combined pressure and flow velocity recordings with microsensors [7, 13]. This provides a complete picture of the haemodynamic of the collateralized territory distal to an obstruction [18, 19]. The assessment of a donor lesion by FFR may be influenced by the myocardial mass distal to the lesion including the collateralized territory. Therefore, physiologically driven revascularization in a donor segment needs to take into account that once the occluded myocardium is reperfused after recanalization, the FFR value may increase and the donor artery obstruction may no longer be below the cutoff value [20, 21].

Collateral function can develop to a similar functional level in patients postmyocardial infarction with large akinetic territories as in patients with normal preserved regional function. Therefore, the presence of viability is not a prerequisite for collateral development and the observation of excellent collaterals should not be the reason to perform the intervention, but rather the proof of viability [22]. On the other hand, the assessment of collateral function shows that the functional competence of collaterals in CTOs is limited even in patients with perfectly preserved left ventricular function distal to an occlusion. During a standard stress protocol with systemic infusion of adenosine the coronary flow velocity and pressure changes distal to an occlusion were well below cutoff values for assessing the functional reserve in non-occlusive coronary obstructions, that is, a flow velocity reserve above 2, and an *FFR* above 0.75. So even well-developed collaterals would not prevent ischaemia during exercise [23].

Collaterals will regress once the native artery that was supplied by the collaterals is revascularized. This process starts immediately after the re-established antegrade flow with immediate loss of collateral conductance, at least with CC1 collaterals, less so with CC2 collaterals. Acute reocclusion, for example, in the course of a late stent thrombosis can therefore lead to an acute coronary syndrome [24, 25], as the recruitment of collaterals is not instantaneous in most patients [26].

For the interventional approach it is important to realize that large epicardial collaterals have in general a lower resistance than septal connections, and thus will be a major source of collateral supply [7]. In case of damage to a collateral bed during an interventional approach that ultimately fails, the ensuing possible myocardial ischaemia will be greater if the major supply is interrupted. Therefore, if the operator has the choice of collateral pathways, he may select the one with the smaller diameter and prefer septal over epicardial pathways. At the same time, it is to be expected that the patient may experience chest pain during the retrograde procedure and this technique needs careful attention to the potential causes of this ischaemia. If no major obstruction is detected, the procedure may be continued despite the discomfort of the patient, and analgesia should be applied.

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Channel Tracking Guidewire and Technique for Retrograde Approach

7

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Evaluation of the collateral circulation is critical for determining the feasibility of the retrograde approach. When assessing collateral channels it is of paramount importance to take time and review the previous angiogram carefully, for multiple potential collateral pathways, as the predominant collateral may change over time prior to the procedure. Careful review of collaterals prior to the procedure can reduce contrast and radiation dose as well as the duration of the procedure.

Retrograde access to the distal vessel can be achieved via septal collaterals, epicardial collaterals (atrial channel), or (patent or occluded) coronary bypass grafts. Generally septals are used more often 65–70% of cases, epicardial 15–20% of cases, atrial 8–10% of cases, and graft 5–8% of cases. In order to identify the best collateral collateral size, tortuosity, bifurcations angle of entry to and exit from the collateral, and distance from the collateral exit to the distal cap should be taken into consideration. Among these parameters the most important predictor of successful guidewire tracking and device crossing is lack of tortuosity, followed by size [1, 2]. The size of the collaterals is often assessed using the Werner classification (CC0: no continuous connection; CC1: threadlike connection; CC2: side branch-like connection) [3].

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7.1 Selecting the Collateral

It is advisable to select a workhorse to reach the proximal entry of the collateral, for three reasons: first is to minimize the risk for proximal vessel injury, second larger tip bends on the workhorse guidewire are often needed to get the proximal entry of the collateral, third the bend to navigate into the collateral is usually small distal bend. Thus, although it might be successful the use of a dedicated guidewire from the start, its distal bend could be compromised for the successful passage in very complex collateral tracking.

There are two techniques for collateral channel tracking: surfing [4] and contrast-guided [5]. Both techniques can be applied to septal crossing, while the latter only to epicardial, saphenous venous graft, and left internal mammary crossing.

7.2 Septal Surfing

It consists of advancing the guidewire through collaterals without contrast visualization, through the beneficial use of the microcatheter. Most of the time, passage of the guidewire is unexpected successful through a septal branch which at first was not visualized. In case of failure these maneuvers can be repeated several times to selectively engage different branches; however, if the wire repeatedly takes the same unsuccessful course, the guidewire should be retracted further back before readvancing to select alternative route. It is important when you surf that you "should take the proper wave," thus never push hard, but stop immediately when you feel resistance; indeed, forcing the guidewire will increase the risk of collateral injury without increasing crossing success. Surfing will be easier in the upper half of left descending artery (LAD) as collaterals are more straight and going more in the direction of the main artery "the wave"; conversely, in the more lower half of LAD collaterals branches will go more backwards and thus more difficult to surf easily. Right anterior oblique (RAO) cranial is the best projections for initial wiring and RAO caudal for entering into the posterior descending artery. Septal collaterals from the most proximal LAD connect to the right posterolateral branch, whereas more distal septal connect to the posterior descending. Finally, very distal septals may connect to a right ventricular branch.

Generally speaking septal collaterals are usually safer and easier to navigate using very soft tip and polymer-jacketed guidewires compared with epicardial collaterals [6, 7].

7.3 Types of Guidewires Used for Surfing

Generally first wires to be used are the Asahi wires and among these the preferred one is Sion, followed by Sion black in case "standard" Sion has some difficulty in channel crossing. In some conditions Sion blue characterized by soft tip could be well used to reduce traumatic danger and when the septal channel is of a reasonable

Table 7.1 Types of preferred wire according to patient type of collateral channel

Type of collateral	Sion	Sion black	XT-R	Suoh 03
Septal CC	Standard	Applicable	Limited	Applicable
Epicardial CC	Applicable	Limited	Very limited	Standard
Atrial or marginal	Applicable	Limited	Very limited	Standard
CC 1 or 2	Standard	Applicable	Applicable	Applicable
CC 0	Applicable	Limited	Applicable	Standard
Unvisualized CC	Limited	Not known	Limited	Applicable
Corkscrew	Limited	Limited	Risk of perforation	Applicable
Rigid epicardial	Limited	Limited	Risk of injury	Applicable

size. Conversely, Sion black due to his polymer jacket coating is very appropriate in case of smaller size, high grade tortuosity, and calcifications (Table 7.1). As an alternative Fielder XTR or Fielder FC could be also used. The new Suoh 03 from Asahi is a dedicated wire for collateral channel crossing; indeed, due to his soft and dedicated characteristic for channel crossing it is often best used with caravel but generally torquability should reserve to only few spins. Furthermore the operator should learn how to progress with this wire into the channel as advancement is totally different from other guidewires and it should be allowed more time to the wire to progress by itself, during diastole and systole of the heart contraction, without pushing and torquing it.

Regarding microcatheters Finecross, Corsair pro, Caravel, Turnpike LP could be used according to operator preferences, diameter and elasticity of the collateral channel.

7.4 Contrast-Guided Septal Crossing

Firstly it is important to cannulate the proximal part of the collateral by the guidewire and by the help of the microcatheter. After removing the guidewire, 100% contrast will be forcefully injected through the help of a small 3 mL, Luer-Lock syringe, into the microcatheter to visualize the collateral vessel course. Remember always to aspirate beforehand to prevent air embolization and to ensure that the microcatheter is not to deeply inside the collateral as this might cause hydraulic dissection and preventing proper visualization course of the collateral vessel. It is always advisable to change tip microcatheter position, more proximally or more distally in order to visualize different branches and focusing better on the proper collateral channel connected with distal retrograde vessel. Injection should be not brisk in the first part of the injection, and rather perform cine-angiography while gently injecting the contrast up-till the end of the one itself contained in the syringe. If a continuous connection to the distal vessel is visualized, it is advisable to reattempt crossing through that connection, but never pan during this maneuver in order to avoid change in collateral road mapping. Consider RAO caudal projection to evaluate the length and tortuosity of the distal part of the septal collateral. Also left anterior oblique projections can be useful if there is limited advancement with RAO views.

7.5 Complications

Collateral dissection might often happen but in most cases further attempts to cross may be performed via a different collateral. Collateral perforations which are nearly benign might cause some localized contrast staining "tattoo"; very rarely there are reported cases of septal hematoma formation and/or perforation into the pericardium causing hemodynamic compromise [8, 9].

Guidewire and microcatheter entrapment might also happen especially if the guidewire and microcatheter are overtorqued by continuous spinning in one direction; generally septal collaterals are more resistant and withdrawal and counterclockwise rotation is preferable to retrieve guidewire and microcatheter [10].

7.6 Contrast-Guided Epicardial Crossing

Similarly to contrast-guided septal crossing performing injection through a microcatheter in order to visualize the collateral vessel course is the gold standard technique. Furthermore, in cases of unfavorable septal collaterals but the presence of a very well developed epicardial branch providing the dominant blood flow to the CTO, balloon occluding the epicardial collateral for 2–4 min may allow recruitment of more favorable interventional septal collaterals that can be used for retrograde crossing. As being epicardial generally more tortuous than septal, selection of the proper microcatheter among the big microcatheters portfolio actually on the market is of paramount importance. To choose the proper microcatheter will allow to select the one with more flexibility in progressing, ones the wire is advancing and also allowing often straightening of the tortuosity allowing subsequent advancement [11]. Rotating the wire and also the microcatheter without pushing in tortuous segments may allow facilitation in crossing the collateral, especially during diastole when the angle between collaterals and turns is wider. In contrast to septal collaterals, which can be safely dilated with small balloons to facilitate microcatheter or device crossing if required, epicardial collaterals should not be never dilated; similarly never let the microcatheter advance ahead of the guidewire as this might cause channel rupture. Sometimes crossing epicardial collaterals can prove impossible, if severe tortuosity and small channel size are the case and in such a condition orthogonal injections are important to determine the collateral vessel course. Finally once the guidewire reaches the distal true lumen it is better to advance it to the distal cap before following with the microcatheter in order to have more support to advance it.

7.7 Types of Guidewires Used for Contrast-Guided Epicardial Crossing

Similarly to septal crossing, Asahi wires are the best ones to be used for epicardial crossing. Among these guidewires Suoh 3 wire performs best in crossing epicardial collaterals, followed by the Sion family. Sometimes in bigger size epicardial channel, Sion wire might be looped distally to increase passage in curly bend and decrease the possibility to engage small branches; however, this is something left to experienced operator and it is never advisable pushing the microcatheter in the back of it before the guidewire passes through (Table 7.1).

7.8 Complications

Sudden myocardial ischemia might develop when epicardial channel collateral is of a big size and generally the only collateral supplying route to the occluded artery; this might also cause sudden arrhythmias and/or hypotension. Similarly to septal channel tracking collateral dissection might often happen but in most cases further attempts to cross may be performed via a different collateral.

Collateral perforations as a cause of channel breakage are rare nowadays, but in such a case can cause quick tamponade which should be reverted promptly together with coiling from both side of the collateral channel. Reported evidence suggests that in post-CABG patients loculated effusions compressing left atrial [12–15] or right ventricle [16] might be life threatening as this cannot be drained by pericardiocentesis. Finally, guidewire tip entrapment of a soft polymer-jacketed guidewire can occasionally happened but generally solved by twisting of the wire and sometime also causing paradox advancement in the channel.

7.9 Bypass Grafts as a Route for Retrograde Approach

Patent bypass graft generally represents an ideal retrograde conduit due to the absence of side branches, predictable course, and large calibers. Even occluded grafts can be used as retrograde pathways. However, in case of collateral circulation originating from the left anterior descending artery, that is supplied by an internal mammary artery (IMA), the access by the IMA graft increases the risk of global ischemia and should be avoided whenever possible [17].

IMA bypass grafts are the least preferred bypass for retrograde wiring as the possible cause of ostial dissection and even antegrade flow cessation and catastrophic consequences if this is the only remaining graft working. In this latter condition a mechanical left assistance device should be strongly considered before starting the retrograde approach.

7.10 Conclusions

Interventional collaterals evolve as technology and expertise evolves. When multiple connections are present, it is preferable to select septal channel as compared to epicardial ones and always evaluating risk/benefit for IMA graft. Sion and Suoh 03 are the default wires, while Sion black, Fielder XT-R are optional excellent wires, that should be always used accordingly over different microcatheters such as Corsair

Pro, Turnpike LP, Caravel, Finecross. In complex collaterals, roadmap selective injection first, drive carefully always torqueing, pushing, and pulling in tune. Success rate of crossing >90% is realistic perspective without increase any complications.

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How to Cross CTO Lesion from Retrograde Approach

8

Hsien-Li Kao

8.1 Introduction

Once the collateral channels (CC) were tracked successfully with retrograde guide wire (GW) and microcatheter (MC) delivered into distal true lumen, the success of the particular chronic total occlusion (CTO) intervention is almost guaranteed. With the current devices and practices, the final technical success could be achieved in up to 90–97% of the cases with successful CC crossing [1, 2]. However, a well-considered and executed plan is mandatory to actually connect the antegrade and retrograde true lumen through the occluded CTO segment. The following chapter will focus on this critical issue of the retrograde CTO PCI in detail.

8.2 Modes of CTO Segment Crossing

In theory, when the MC is delivered into distal true lumen, the CTO segment may be crossed in 4 patterns of wire connections [3]. The antegrade wire may be manipulated, using the retrograde wire engaged in the CTO segment as a landmark, to cross the lesion. This pattern is usually referred to as "kissing wire crossing," however, and should be considered as an antegrade CTO crossing mode and will not be further discussed here. Other CTO segment crossing modes will be described in detail in the following, including retrograde wire crossing, controlled antegrade and retrograde sub-intimal tracking (CART), and reversed CART.

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8.2.1 Retrograde Wire Crossing

When MC enters the distal true lumen, the operator can switch the collateral crossing wire, usually a soft wire such as Sion or Suoh03, into a moderate/high stiffness steerable wire to engage the distal fibrous cap. Similar to the antegrade approach, choice of the initial retrograde wire is dependent on the morphology and expected/actual hardness of the cap, as well as the existence of connecting micro-channels in the occlusion segment. Wire de-escalation may be needed in the CTO body for better loose tissue tracking and precise advance inside the intra-plaque position. As the operator is now handling the wire over a long distance across the donor-collateral-receiver vessel loop, good torque transmission and response is necessary. When finally approaching the proximal cap, the wire may also need to be escalated to puncture through into the proximal true lumen. When successful, this mode of CTO crossing is defined as retrograde wire crossing (RWC) and can be very time and resource efficient. But as the operator is controlling the wire from a long distance in RWC, the precision and force delivery would be compromised. Excessive maneuvering in RWC mode may thus create large false lumen or hematoma, making the transition to other crossing modes difficult. Therefore, the operator should not be too obsessed with RWC, unless certain features described in Sect. 8.3 exist.

8.2.2 Controlled Antegrade and Retrograde Sub-intimal Tracking

This method, abbreviated as CART technique, was first described by Japanese authors [4]. In brief, a balloon is brought down through the CC over the retrograde wire already engaged into the CTO, and inflated inside the occlusion body. Thus a localized sub-intimal dissection is created, resulting in a space when the balloon is deflated. The antegrade wire is then maneuvered from proximal true lumen into this sub-intimal space within the CTO segment, and subsequently into the distal true lumen and completes the CTO crossing. Obviously, this technique requires some prerequisites to be successful. Firstly, as the CART balloon must be delivered through the CC, the size and tortuosity of the channel must be favorable. This is especially important considering the retrieval of the balloon after inflation and deflation, as the profile must be bulkier and may cause CC trauma. Secondly, when pushed against resistance, the shaft of a rapid-exchange design balloon will separate at an angle from the wire it is tracking. This "scissoring" effect may result in severe CC injury or even laceration. Therefore, a small profile over-the-wire design balloon is better suited for this application. Even with these conditions are fulfilled, there are still issues to be concerned. There is very limited information to guide the choice of adequate size of the balloon and appropriate position for inflation, even with bilateral injection angiography or intravascular ultrasound (IVUS). Therefore, with the potentially increased risk and technical uncertainty, CART technique is used only in a small portion of procedures in the modern era of retrograde CTO PCI [5–7].

8.2.3 Reverse Controlled Antegrade-Retrograde Technique

Abbreviated as r-CART, this technique was first described by Japanese authors [8]. A balloon is advanced into CTO segment over the engaged antegrade wire. Inflation is then carried out to create a localized sub-intimal dissection in the CTO segment. The retrograde wire, supported by the MC, is then advanced from the distal true lumen into the dissection space, and finally into the proximal true lumen. This technique is made possible with the introduction of modern MC like Corsair (Asahi Intecc, Aichi, Japan), and highly controllable wires with proper stiffness for the retrograde direction. As the balloon is delivered via antegrade system, the risk of injuring CC and uncertainty about the balloon size is non-existent. Furthermore, when initial r-CART attempt failed to connect antegrade and retrograde wires, it is very easy to start IVUS examination from the antegrade wire, to evaluate the situation. As explained by Sumitsuji et al. [3], understanding the positions of both ante- and retrograde wires and histo-pathological characteristics of the tissues within the occlusion is important for the choice of further actions. This will be discussed in detail later.

8.2.4 Definition and Terminology of Different r-CART Variations

To achieve the “conventional” r-CART, a relatively long longitudinal overlapping of the ante- and retrograde wires must be established. The concept is to inflate the balloon over the antegrade wire, alongside the overlapping retrograde wire, so that a space is created connecting both wires. Obviously when the occluded segment is tortuous or calcified, or when its course is ambiguous, bilateral wiring for overlapping will be tedious and technically demanding. Increased time, resource, radiation, and contrast usage will be an issue, as well as the increased risk of complications. A relatively large diameter balloon is usually used to maximize the chance of creating connection between wires, thus also increase the vessel trauma and potential perforation risks. Occasionally, the proximal or distal fibrous caps can be too hard to be penetrated by either the wire or MC/balloon, and r-CART is not possible despite wire overlapping. A few variations to the “conventional” r-CART had thus been proposed and clearly described [9].

8.2.4.1 “Directed r-CART”

This technique may minimize vessel trauma and expedite the procedure with the use of retrograde wires with excellent directional control and penetration efficiency, such as the Gaia series (Asahi Intecc). Antegrade preparation is first done with wiring into the occlusion segment up to 5–10 mm proximal to the distal cap. Retrograde approach is then commenced until the retrograde wire is engaged inside the occlusion, keeping the wires as coaxial and distance in-between as minimal as possible. Wire overlapping is not necessary, and excessive manipulation should be avoided. A small (usually 2 mm) balloon is then brought down over the antegrade wire and inflated, and the retrograde wire is advanced toward the end of the antegrade balloon. While deflating the antegrade balloon, the retrograde wire is gently pushed to puncture into the space created and completes occlusion crossing. This technique is recommended for its efficiency and safety, but in CTO's with proximal cap ambiguity, tortuous or uncertain occlusion course, other techniques may be more appropriate.

8.2.4.2 "Extended r-CART"

This technique may be applied when antegrade preparation or retrograde cap penetration is not possible due to extreme cap tissue hardness. If the proximal cap is too hard, the antegrade wire is pushed into sub-intimal space proximal to the cap. If retrograde cap is too hard, the antegrade wire is advanced beyond it. The antegrade balloon is then actually inflated proximal or distal to the edge of the occluded segment, and the dissection space thus created is extended beyond the occlusion longitudinally. Thereafter, the retrograde wire is advanced through this space to achieve connection between the proximal and distal true lumen, "bypassing" the impenetrable cap. This technique inevitably results in sub-intimal (at least partial) stenting and longer total stent length. It is noteworthy, in addition, that significant branches between the sites of the extended r-CART and the cap may be lost after stenting of the extended sub-intimal dissection. These two drawbacks are similar to those of the antegrade dissection reentry (ADR) technique and should be considered carefully.

8.2.5 Knuckle Wire Technique

When the length of the occluded segment is long, especially with ambiguous or tortuous course and/or heavy calcification, wire manipulation of the retrograde wire would be extremely difficult and time-consuming. The excessive manipulation of the retrograde wire results in large hematoma and increased risk of perforation. Knuckle wire technique (KWT) from the retrograde direction is highly efficient and safe in this situation [10]. Pushing a retrograde polymer-jacketed wire inside the occlusion to form a knuckle, and allow the knuckle to track the sub-intimal space with continuous push, will delineate the occlusion course safely and quickly. The support of the knuckled wire also facilitates the delivery of retrograde MC into the CTO segment, for exchange to the wires to finish r-CART.

8.3 Algorithm of Initial Crossing Mode Choices

With all the techniques and devices available, the operator is often left with the question of "which technique to start with." A structured and algorithmic decision process on the initial approach, based on angiographic and IVUS characteristics, will provide an efficient and fluent procedure. This is especially important for the young operators in their learning curve, to prevent both unnecessary exhaustion and complication. A good example is the "APCTO Retrograde Algorithm" (Fig. 8.1) [11]. As it pointed out, the majority of retrograde CTO would be crossed with r-CART, using the techniques described in the previous section. But two exceptions should be recognized early on in the procedure.

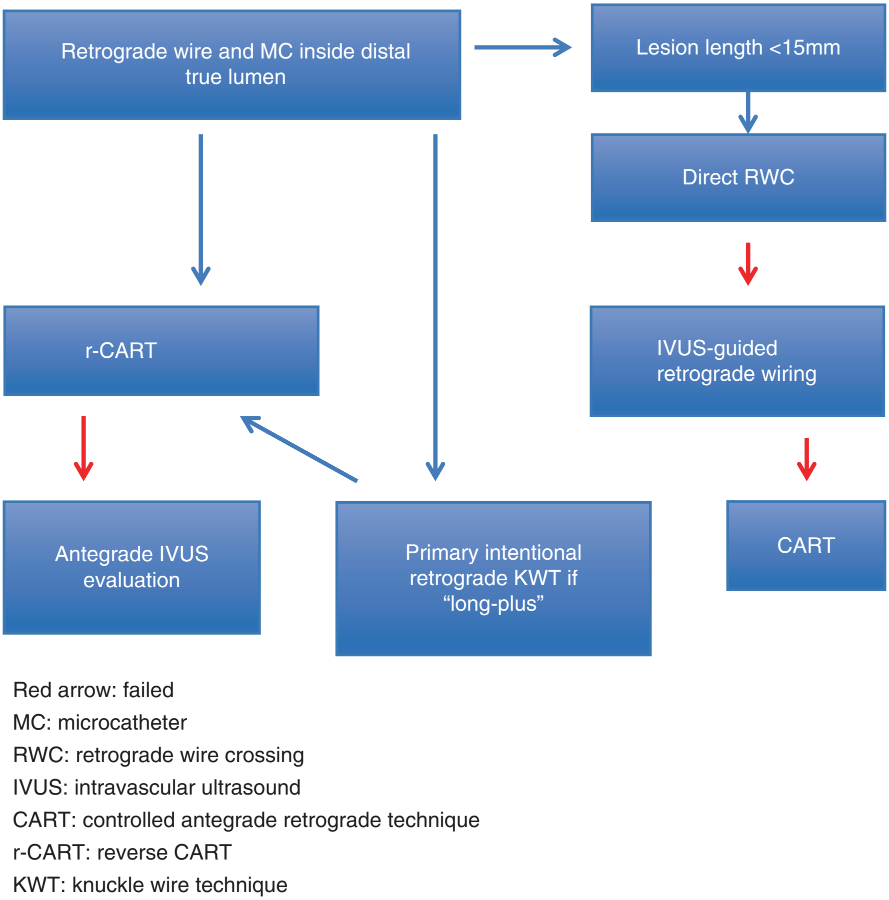

Fig. 8.1 Asia Pacific Chronic Total Occlusion club (APCTO club) algorithm for retrograde crossing approaches (adapted and modified from [11]). Red arrow: failed, *MC* microcatheter, *RWC* retrograde wire crossing, *IVUS* intravascular ultrasound, *CART* controlled antegrade retrograde technique, *r-CART* reverse CART, *KWT* knuckle wire technique

8.3.1 The Short CTO

A simultaneous injection from both the antegrade guide catheter (GC) and retrograde MC should be performed once the retrograde MC is delivered into distal true lumen through IC. Sufficient contrast filling and exposure will demonstrate the real occlusion length and the morphology of the distal cap. The true occlusion is usually shorter than expected. If the occlusion length is less than 15 mm, and the distal cap morphology is favorable, i.e., concave towards the occlusion and not heavily calcified, direct RWC is recommended. Retrograde wire escalation or de-escalation among the modern CTO wires of good torque response and tip stiffness, such as the Gaia series, is similarly important as in antegrade wire crossing. If the CTO is located in ostial LAD or LCX, care must be taken when the retrograde wire is approaching the proximal cap. If the retrograde wire fails to cross clearly through the cap into proximal true lumen, but instead deviates off the cap and is advanced into sub-intimal space proximally, the other major branch vessel will be compromised. Therefore a wire in the other branch for protection is recommended in this situation. The operator can also use IVUS over the side branch wire to guide the manipulation of the retrograde wire crossing of the proximal cap.

8.3.2 The "Long-Plus" CTO

The length of the CTO segment itself is not indicative of wiring difficulty, nor dictates wiring strategy. But when certain features such as tortuosity, heavy calcification, or course ambiguity coexist, retrograde crossing of the CTO with traditional wiring technique will be very difficult and unpredictable. Not only time and resource consuming, the excessive manipulation will create large hematoma and possibly extravasation. In this situation, the so-called long-plus CTO, antegrade preparation to achieve ante- and retrograde wires overlapping for the r-CART is also difficult. An intentional application of the KWT from the retrograde direction is the best solution in the long-plus CTO scenario. The ambiguous course of the CTO can be delineated quickly, and the tortuosity or calcification can be bypassed safely. It is of note that KWT is better applied from the retrograde but not the antegrade direction, as an antegrade knuckle can easily migrate into side branch at bifurcation within the CTO. If applied from retrograde direction, due to the usually reverse angle, the knuckle seldom migrates into side branch, but most likely stays in the main vessel structure and continues moving proximally. Once the knuckle reaches the proximal cap, the retrograde MC is advanced, the knuckle wire is exchanged to another retrograde wire for RWC or r-CART.

8.4 Bailout of Initial r-CART Failure

When the initial r-CART attempt failed to connect the wires, it is imperative to use IVUS to evaluate the situation before deciding the next step. Proper dilatation of the proximal cap with small balloon may be needed to facilitate IVUS probe delivery. An imaging catheter with better distal reach, such as the EagleEye (Vulcano, San Diego, CA, USA), is recommended [12]. The possible positions of both the ante- and retrograde wires in a failed r-CART scenario may be any one of the following: (1) ante-intra-plaque and retro-intra-plaque; (2) ante-intra-plaque and retro-sub-intimal; (3) ante-sub-intimal and retro-intra-plaque; and finally (4) ante-sub-intimal and retro-sub-intimal. But practically it is unnecessary to classify the wires positions into such details, as the subsequent proper actions may not be different. In addition, clear visualization of the retrograde wire may sometimes be difficult. Therefore, a simplified and algorithmic approach was proposed by the APCTO Club (Fig. 8.2) [11].

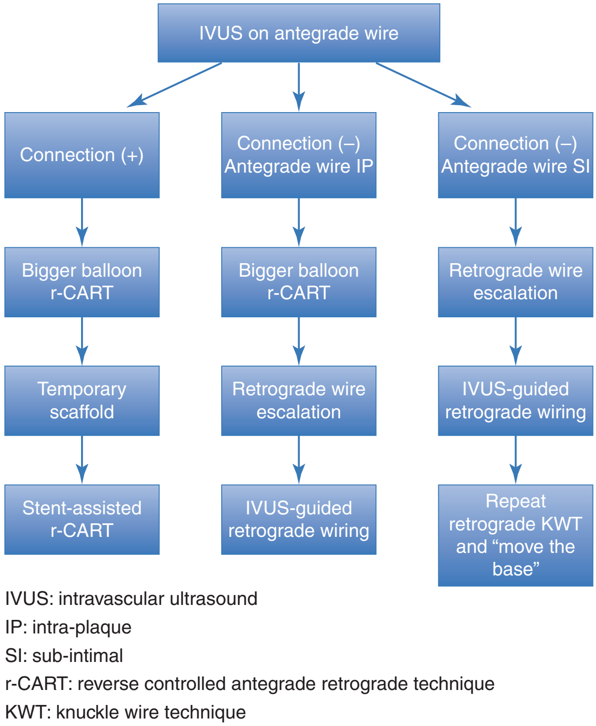

Fig. 8.2 Asia Pacific Chronic Total Occlusion club (APCTO club) algorithm for IVUS guided r-CART (adapted and modified from [11]). *IVUS* intravascular ultrasound, *IP* intra-plaque, *SI* sub-intimal, *r-CART* reverse controlled antegrade retrograde technique, *KWT* knuckle wire technique

8.4.1 Connection Between both Wires Confirmed

In this situation, both wires are actually already in the same space, but the residual tissue in-between is obstructing the wire passage. Further larger balloon r-CART will usually be successful. If this still fails, the most common cause is the retrograde wire being caught up by the dissection/tissue between the connection point and the proximal true lumen. If retrograde MC can be advanced into the occlusion segment, the active retrograde wire may be exchanged to a new workhorse wire for better maneuverability. Other methods to overcome this situation include:

- *Guide extension*: A GC extension device, such as Guidezilla (Boston Scientific, Marlborough, MA, USA), can be advanced through the antegrade GC to approach close to the connection point. This will provide coaxial route and temporary scaffold for the retrograde wire passage.
- *Other temporary scaffold*: An antegrade balloon may be used as temporary scaffold. It is first delivered over the antegrade wire, inflated close to the tip of the retrograde wire. While deflating the balloon, the retrograde wire is advanced proximally through the temporary void. This maneuver can be repeated in more proximal positions until the retrograde wire finally reaches proximal true lumen. Soutenir device (Asahi Intecc) or other on-the-wire micro-basket may also be used as temporary scaffold.

- *Stent-assisted r-CART*: A stent can be deployed with its distal edge at the connection point. The stent will thus provide permanent scaffold for the proximal luminal space. This is the last resort in this scenario, and may not be feasible in certain situations such as short RCA ostial occlusion.

8.4.2 No Connection and Antegrade Wire Intra-plaque

When IVUS confirmed that the antegrade wire is inside the plaque (or inside the intima space) but there is no connection yet between both ante- and retrograde wires. In this situation, the initial r-CART did not create a deep enough fissure inside the plaque tissue to connect both wires, or the internal elastic lamina is not fractured to connect the intra-plaque antegrade wire and sub-intimal retrograde wire. Therefore, the following step is to simply repeat r-CART using a larger balloon, according to the IVUS estimation of the reference vessel size. In combination, the retrograde wire may also be exchanged to a stiffer wire with higher penetration force to puncture towards the antegrade space, with or without real-time IVUS guidance.

8.4.3 No Connection and Antegrade Wire Sub-intimal

This is a more difficult condition, when the antegrade wire is sub-intimal and retrograde wire intra-plaque. Using a larger balloon to repeat r-CART is not advisable, as it is difficult to rupture the internal elastic lamina from the sub-intimal space with large balloon inflation. Instead, repeat r-CART with larger balloon will expand the sub-intimal space further, creating large hematoma and increasing the risk of adventitia injury and vessel perforation. The proper next step is to exchange the retrograde wire to a stiffer higher penetration force wire to puncture towards the antegrade space, better with real-time IVUS guidance. The other alternative is to move the position of the following r-CART along the vessel long axis, where both wires are in the same potentially connecting space. This can be achieved easily by pulling back the retrograde wire and intentionally applying retrograde KWT. A polymer-jacketed wire such as Pilot 200 (Abbott Vascular, Santa Clara, CA, USA) will move easily into sub-intimal space, allowing the retrograde and antegrade wires to be located in the same potentially connecting space. After IVUS confirmation, subsequent r-CART can be carried out just as described earlier.

8.5 How to Establish the "Rail"

When the retrograde wire enters the proximal lumen, the CTO crossing is complete. But further balloon dilatation and stent delivery over the retrograde wire via CC is practically impossible. The proper subsequent steps to establish the "rail" for final stent deployment will be described in the following:

8.5.1 Externalization

This is the current recommended default. The retrograde wire is advanced into the antegrade GC, or lumen of the GC extension. Then a balloon is inflated inside the antegrade GC to trap the wire tip, providing strong support for the retrograde MC to be advanced across the occlusion into the antegrade GC. The trapping balloon is then released and retrograde wire exchanged to an externalization wire, such as RG3 (Asahi Intecc). The externalized wire is advanced continuously until its tip exits the hemostatic valve of the antegrade MC. Now the operator has both ends of the externalization wire at hand, and the subsequent devices can be delivered from antegrade direction like routine intervention procedure with excellent wire support. In case the operator wishes to have another antegrade wire for further device delivery, a double lumen catheter over the externalized wire should be used for safe and guaranteed transition. This practice is necessary when the subsequent balloon or stent deployment may involve vessel segment close or distal to the confluent point where the CC joins the distal true lumen. Once the antegrade wire is in place, the externalized wire should be removed before stent deployment, to avoid jailing and subsequent complications.

8.5.2 Snaring

There are situations where the retrograde wire cannot be advanced into the antegrade GC, despite coaxial GC position and use of guide extension. If the wire can be advanced into the ascending aorta, pulling the retrograde wire into antegrade GC with snares is the intuitive next step. However, this should be done carefully and methodologically to prevent potentially unsolvable technical complications. Failure to release the snared wire inside antegrade GC and failure to pull out the wire bent by snare into retrograde GC are both impossible to bail out except for open surgery. The recommended way of snaring is explained as following:

- *Exchange retrograde wire*: The retrograde wire should be advanced as far as possible into ascending or even descending aorta, to provide support for retrograde MC passage across the occlusion. Once the retrograde MC is inside proximal true lumen, the retrograde wire is exchanged to RG3. The long wire length allows for snaring position away from aortic arch, to prevent the risk of potential embolic stroke. The soft and elastic shaft also reduces the risk of failure to release or pull through.
- *Position of snaring*: a just distal to the left subclavian artery takeoff. A 3-lobed (En Snare, Merit Medical, South Jordan, UT, USA) or gooseneck type (Amplatz snare, Medtronic, Minneapolis, MN, USA) snare through the retrograde GC is open and placed perpendicular to the trajectory of RG3, which is advanced into the snare loop. The snare is then closed gently to catch the radio-opaque portion of RG3. Once the grasp is achieved, the snare and RG3 are pulled/advanced together into the retrograde GC, and the snare released. The RG3 will be further advanced just like described in Sect. 8.5.1.

8.5.3 Rendezvous Technique

The operator may choose not to apply externalization after retrograde MC being positioned inside antegrade GC. Instead, the retrograde wire is pulled back partially, leaving the distal end of retrograde MC open. A bare antegrade wire is then advanced directly into the retrograde MC. This is actually easy, if the distal end of retrograde MC is positioned in the curved area of the antegrade GC, with a new and properly shaped modern workhorse wire [13]. The antegrade wire is advanced through the retrograde MC beyond the confluent point of CC and distal true lumen, and then the retrograde MC is retracted. The antegrade wire is now free to access the distal true lumen and complete the procedure.

8.5.4 Tip-In Technique

Sometimes the operator cannot advance the retrograde MC into antegrade GC, despite trapping of the retrograde wire. Exchange of the retrograde wire to RG3 is also impossible. In this situation, an empty MC may be placed inside the antegrade GC with its tip parked at the curved segment. The operator now can manipulate and advance the retrograde wire into the open antegrade MC. This is called *Tip-in* and can be considered a reversed *Rendezvous*. The antegrade MC can now be advanced over the retrograde wire across the occlusion. Once the antegrade MC is inside distal true lumen, the retrograde wire is withdrawn and antegrade wire can be delivered through the antegrade MC.

8.6 What if the Proximal Cap Is Non-Penetrable?

All the above procedures and techniques are based on the assumption that antegrade preparation is achieved, with wire penetrated the proximal fibrous cap, and devices such as balloon and IVUS delivered successfully. However, there are clinical situations where the cap is too tough to be penetrated by even the hardest wire. Techniques or maneuvers enhancing support to the penetrating wire, such as side branch anchoring and guiding catheter extension, may help solving the first scenario. If all failed, operator can apply the so-called scratch and go technique to enter sub-intimal space intentionally proximal to the cap and proceed as described in Sect. 8.2.4.2. There are also situations that the cap tissue is too resistant for device delivery despite all maneuvers to enhance support. In this condition, balloon-assisted micro-dissection [14] may be helpful to “shake loose” the cap tissue for later device delivery. Alternatives also include the use of rotational atherectomy on a cut Rotawire (Boston Scientific) advanced via antegrade MC in exchange of the penetrating wire, or Excimer laser (Spectranetics, Colorado Springs, CO, USA) ablation, if the devices and expertise are available.

8.7 When to Abort

A good operator should always know when to stop and accept a failed procedure. The rule of 3-4-5 proposed by the APCTO Club algorithm is a reasonable and practical guideline [10]. The intervention should be terminated, unless well progressed, if the procedure time is already 3 h, or the contrast volume exceeds 3.7 times of patient eGFR, or radiation exposure exceeds AirKERMA 5Gy. A patient can always be brought back on the table next time, and instead, unreasonable persistence will lead to complications and catastrophe.

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9 The Concept of Algorithm Approach in CTO PCI

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Despite years of evolutions and advances of coronary intervention, percutaneous coronary intervention (PCI) in chronic total occlusions (CTOs) remains technically complex and challenging [1–4]. It is considered as one of the last frontiers in coronary intervention [5]. In the modern era, technical success rates of CTO PCI have been improved from 50 to 70% [6, 7] to over 90% in some high-volume centers and well experienced operators due to the development of CTO equipment and techniques. Success rates vary a lot in different centers and operators [3]. So, it is of great significance to integrate these techniques together to form a comprehensive procedural strategy for further improvement of success rate in CTO PCI of the worldwide.

9.1 Significance of Algorithm Approach

PCI in CTOs is generally complex and becoming a proficient CTO operator requires dedication, perseverance, and preparedness with a high upfront investment in amount of time, energy, and resources, with a relatively long learning curve in beginners or not experienced CTO interventionalist. Thereby, a systematic algorithm based on accumulated experiences is essential to create a basis process whereby operators could follow to react to angiograms and craft strategies in a similar manner.

The algorithm for PCI in CTOs was initially reported in 2012 via consensus based on the expert opinion of 13 high-volume North American CTO operators [8], now commonly referred to as the hybrid algorithm. This hybrid algorithm had

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become the basis for discussion and reference of CTO PCI in the worldwide, which used the angiographic characteristics to guide selection of the initial crossing strategy and encouraged early conversion to an alternative strategy in case that the initial strategy failed. However, this hybrid algorithm only describes the overall approach to crossing these lesions, failed to cover technical challenges which can occur during implementation of these various approaches. Moreover, compared with North America and Europe, substantial variations in practice patterns lie in CTO PCI approaches in the Asia Pacific region where most of the world's population resides because of several reasons below. Firstly, the traditional wire-based CTO teaching is dominant in the region, and antegrade dissection re-entry arm of the hybrid algorithm is eliminated. Secondly, lower rates of coronary artery bypass grafting [9, 10] also contributed to the differences in CTO PCI approaches.

In 2017, the Asia Pacific CTO club, a group of 10 high-volume CTO operators who are recognized as leaders in CTO intervention in their respective countries, proposed a new algorithm for CTO PCI applicable in the worldwide [11], on the base of hybrid algorithm and combined with the actual conditions of Asia Pacific region. The new algorithm highlighted the role of intravascular ultrasound (IVUS)-guided entry to overcome proximal cap ambiguity, detailed the indication of antegrade dissection re-entry with the Stingray System (Boston Scientific), and guided when to stop a procedure. Furthermore, total occlusion of in-stent restenosis (ISR) is separated into a distinct category with recommendation of use of CrossBoss as the primary crossing strategy in the new algorithm [11].

On the base of hybrid algorithm in 2012 by North American CTO operators and the new algorithm in 2017 by Asia Pacific CTO club, Chronic Total Occlusion Club in China comprised of dozens of high-volume and experienced CTO operators recognized as leaders in CTO intervention in China proposed a Chinese-specific algorithm approach for CTO PCI in 2018.

The goal of these three algorithms above is to combine technologies and techniques in a way that facilitates opportunities to attempt CTO PCI in patients with appropriate clinical indications irrespective of anatomy. These algorithms allow for differing skill sets and equipment availability and have been proven to improve the intervention efficacy and procedural success rates of complex CTO lesions, which are reproducible and teachable. Furthermore, these algorithms contain practical teachings for CTO PCI, aim to provide a standardized tool for education and training and avoid futile strategies. It is hoped that these algorithms will serve as the basis for future CTO PCI proctoring and training.

9.2 Image Review and Evaluation

Detailed evaluation of CTO lesion and careful reading of coronary angiogram are the cornerstones of interventional therapy in CTOs [12]. Multi-angle and bilateral coronary angiography are required for most CTO lesions before interventions [13]. As for CTO lesions with good collaterals, bilateral coronary angiography or super-selective angiography via ipsilateral collateral vessels is recommended to reduce the injury of antegrade contrast-injection to the target vessels during interventional therapy [14]. Coronary computed tomography angiography (CCTA) is recommended before re-intervention in previous intervention failure or CTO lesions with complex anatomical structures (for example, severe tortuosity, abnormal origin, complete occlusion of ostial). Pre-procedural CCTA could provide information about the vessel course in the occluded segment, including calcification, lesion length, stump morphology, presence of side branches, and post-coronary artery bypass grafting anatomy, which may not be provided by invasive angiography and may improve procedural success in complex CTO PCI [15].

Routine "ad hoc" CTO PCI was not encouraged because pre-planning facilitates a thoughtful procedural approach and estimation of the risk–benefit ratio in this complex lesion/patient subset. In the image evaluation of CTO lesion, we should focus on the anatomical structures of proximal segment of CTO (stump morphology, presence of major side branches at site of the proximal cap), middle part of CTO (calcification, tortuosity, length of occlusion), and distal segment of CTO (morphology of distal fibrous cap, presence of major side branches at site of the distal cap, and diffused lesions in distal vessel) [12]. In addition, the presence of appropriate collaterals should be carefully assessed, including the origin of collateral channels, lumen diameter, degree of tortuosity, angle of collateral vessels to donor/recipient vessels, and the distance of the collateral channels to the occlusion from the site of joint of recipient vessels [12, 14]. Severe lesions in donor vessels should be treated before retrograde intervention, in case of possibility of influence of the blood flow or acute occlusion in the process of retrograde intervention.

9.3 Strategy Planning of CTO PCI

9.3.1 Initial Strategy Algorithm of CTO PCI

Antegrade interventional therapy is recommended for CTO lesions with tapered stump in initial strategy. Accurate identification of the proximal cap is essential to allow safe and successful antegrade strategy. In case of ambiguity of the proximal cap, the antegrade strategy can be performed under the guidance of IVUS (if possible). IVUS can also provide information regarding the composition of the cap and can help to guide the choice of initial antegrade wire.

Strategy of antegrade dissection re-entry (ADR) [16–19] can be used in case of previous failure of antegrade intervention, inappropriate collaterals, previous failure of retrograde intervention, good landing zone of the target coronary vessel at the distal cap, absence of major side branches and with length of the occlusion greater than 20 mm.

As for CTO lesions not suitable for antegrade strategy, retrograde strategy could be performed directly if there are appropriate collaterals. Favorable collateral channel characteristics for retrograde strategy include minimal tortuosity, sourcing from a healthy (or repaired) donor vessel, entering the CTO vessel well beyond the distal cap, easily accessed with wires and microcatheters, not the only source of flow to the CTO segment (with risk for intraprocedural ischemia). More available collaterals lower the barriers and make it easy to utilize retrograde approach as an initial strategy.

9.3.2 Strategy Adjustment and Conversion in the Process of CTO PCI

The key of strategy adjustment during the procedure is to timely conduct the strategy conversion. Rapid adjustments and change of strategies will ensure safety, efficiency, and effectiveness and maximize the likelihood of procedural success.

If the antegrade wire escalation failed to pass through the occlusion, the ADR technique or parallel wiring technique could be considered for strategy conversion. For the purpose of increasing the success rate of parallel wiring technique, the dual-chamber microcatheter can be used, such as KDLC (Kaneka Corporation) or SASUKE (ASAHI INTECC CO., LTD.) dual-chamber microcatheter (Fig. 9.1).

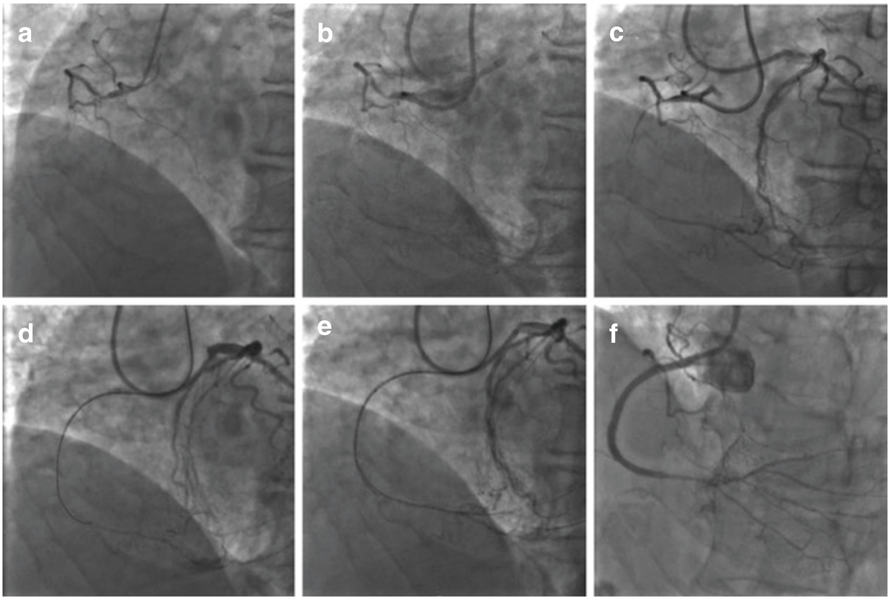


Fig. 9.1 Anterograde approach using the parallel wire technique in recanalization of right coronary artery (RCA) CTO. (**a**) CTO in proximal RCA with a tapered stump at proximal cap. (**b**) Bilateral contrast injection revealing CC2 septal collaterals from the left anterior descending (LAD) coronary artery with diffused lesion at distal cap with a length of occlusion of more than 20 mm. (**c**) A Fielder XT wire (Asahi Intecc, Japan) supported by a Corsair microcatheter (Asahi Intecc, Japan) was started. (**d**) Antegrade wire escalation technique with try of an Ultimate Bro 3 wire (Asahi Intecc, Japan), a GAIA second wire (Asahi Intecc, Japan), and a GAIA third wire (Asahi Intecc, Japan) made progress through the body of the occlusion but clearly appears to have deflected from the target. (**e**) A Fielder XT-A wire (Asahi Intecc, Japan) is advanced parallel to the GAIA third wire supported by a KDLC (Kaneka Corporation) and steered towards the distal end of the occlusion. Successful chronic total occlusion (CTO) crossing confirmed by contralateral angiography. (**f**) Final angiographic result after implantation of 3.0 × 38 mm and 3.5 × 33 mm everolimus eluting stents

If there were severe diffuse lesions in the target coronary vessel at the distal cap, the success rates of parallel wiring technique and ADR technique tend to be deducted. Hence, early initiation of retrograde strategy is recommended if the collaterals are available.

Hybrid strategy combined antegrade and retrograde approach should always be prepared. Sole antegrade or sole retrograde strategy can hardly be achieved in complex CTO lesions. Hence, the retrograde strategy is recommended to be started early after failure of antegrade attempt, or retrograde strategy should be initiated directly, and ADR technique can be used together in part of cases.

9.4 Pre-Procedural Preparation of CTO PCI

The access of interventions should be selected and determined according to basic status of patients, operators' habits, techniques and instruments to be used, and so on [20]. Under the premise of ensuring coaxial, it is recommended to use the guide catheter with strong active support as far as possible. In case of use of IVUS for real-time guidance, 7F guide catheter is recommended for least. 8F guide catheter is recommended if KDLC dual-chamber microcatheter and IVUS are planned to use together. If you failed to use 8F guide catheter, but the dual-chamber microcatheter is a necessary for interventional therapy under the guidance of IVUS. If 8F guide catheter is unavailable and dual-chamber microcatheter is necessary, SASUKE dual-chamber microcatheter can be an option, as well as Ping-Pang guide catheter technique. 7F or 8F guide catheter is recommended when using ADR instrument. Guide catheters with side holes would help to reduce coronary artery ischemia and the occurrence of coronary artery injury caused by contrast injection. In order to prevent the formation of thrombus in catheter, the routine use of heparin as anticoagulation and regular monitoring of activated clotting time (ACT) are recommended in the process of CTO PCI. ACT should be monitored every 30–45 min, maintained from 250 s to 350 s.

9.5 Technique Used in CTO PCI

9.5.1 Antegrade Technique of CTO PCI

9.5.1.1 Wire Selection and Escalation of Antegrade Approach

1. As for CTO lesions with partial recanalization of visible channels, it is recommended to start with a tapered polymer jacketed wire with a low tip load. The tapered tip facilitates entry into the microchannel, the polymer jacket enhances lubricity and trackability, and the low tip load reduces the likelihood of the guidewire exiting the microchannel. The wire should be escalated to moderate or high tip load if failure to pass through the occlusion lesion.
2. As for CTO lesions with tapered stump at proximal cap, it is recommended to start with a tapered wire with low penetration force because a tapered morphology

often indicates that the occlusion is more recent and has a softer composition [21]. If this is unsuccessful, then escalation to an intermediate penetration force guidewire should be undertaken, or to a high penetration force if necessary.

3. As for CTO lesions with blunt stump or with no obvious stump, a wire with intermediate penetration force should be initiated in combination with a microcatheter with good penetration properties, because a blunt morphology often indicates that the occlusion is older and is likely to have a tougher composition. If penetration is unsuccessful, we should escalate to a high penetration force guidewire. After penetration through the proximal cap, the high penetration force guidewire should be stepped down to an intermediate penetration force and non-tapered guidewire to reduce the risk of perforation and increases the chance of tracking the vessel in case that the occluded segment is long, or the travel route is not clear. Once the guidewire reaches the distal cap, it should be stepped up a high penetration force guidewire with good manipulation performance to puncture through the distal cap into the distal true lumen. Use of Gaia series guidewire (ASAHI INTECC CO., LTD.) should be prudent in lesions with severe calcification, tortuosity, and long occlusion.
4. As for CTO lesions with ambiguity of the proximal cap and appropriate branch exists closest to the region of the proximal cap, IVUS should be placed in the branch nearest to the proximal cap and withdrawn to guidewire penetration of proximal cap (Fig. 9.2). Contrast angiography should be undertaken when the IVUS is next to the CTO proximal cap and then we can then use the angiogram to guide the site of proximal cap.

9.5.1.2 Antegrade Guidewire Technique

During the antegrade approach, it is recommended to use the guidewire escalation technique first in case of short length of occlusion. If the occluded segment was long or the guidewire escalation technique failed, ADR technique should be considered in case of good landing zone without major branches involved, including CrossBoss

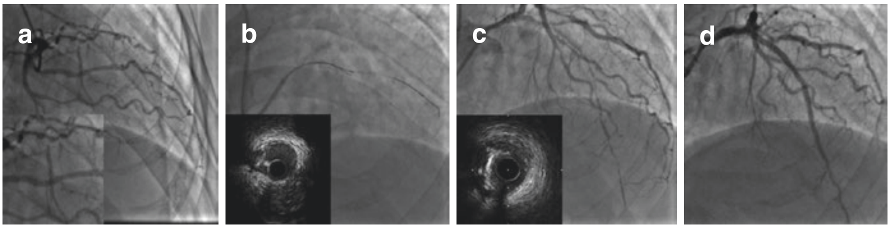


Fig. 9.2 IVUS-guided antegrade approach in recanalization of left anterior descending (LAD) CTO. (**a**) Stumpless proximal LAD occlusion at the takeoff of a big first diagonal branch (D1). Left circumflex artery (LCX) providing retrograde flow to the occluded LAD via epicardial collaterals. (**b**) IVUS catheter (Boston Scientific, USA) in D1 identifying the proximal CTO cap. Following IVUS guided puncture of CTO proximal cap with Crosswire NT (Terumo, Japan). (**c**) The guidewire running through to the distal of LAD and IVUS confirmed in the true lumen. (**d**) Final angiographic result after a 2.5 × 30 mm, a 2.5 × 38 mm, and a 3.0 × 38 mm everolimus eluting stents implantation

(Boston Scientific Corporation) (Fig. 9.3) and Stingray (Boston Scientific Corporation) (Fig. 9.4) system [16, 17] or subintimal tracking and re-entry (STAR) technique [18, 19] based on guidewire. As for part of the cases, the guidewire can be manipulated from false lumen into true lumen under the guide of IVUS. If the ADR technique is unavailable, the parallel wiring technique or retrograde guidewire technique can be adopted. If the antegrade guidewire technique failed, the retrograde strategy should be performed as soon as possible, in the presence of appropriate collaterals.

When the wire crosses the lesion, but the microcatheter or balloon cannot follow, the solutions to this problem are listed as below after verification of guidewire in the distal true lumen. This situation is most commonly seen in a heavily calcified and/or post-CABG lesion. Deep intubation of the guide catheter can provide extra active support but is limited by the possible occurrence of the dissection of proximal plaques or total occlusion of the vessel during maneuvers of this type. Alternative methods to augment guide catheter support include "mother and child" catheter (such as The Heartrail system, Terumo, Tokyo, Japan) and other various coaxial

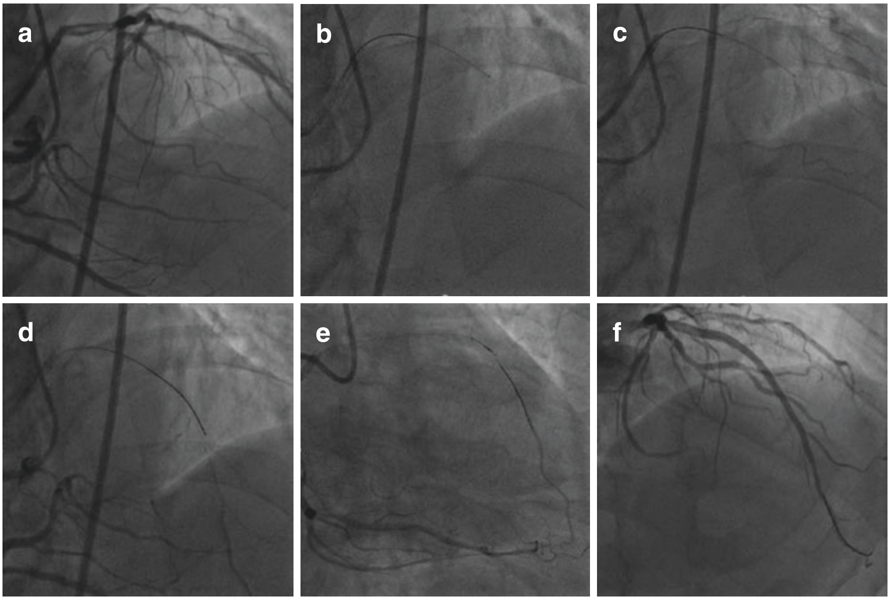


Fig. 9.3 Antegrade approach using ADR technique in recanalization of LAD CTO. (**a**) Bilateral coronary angiography demonstrating a mid-LAD CTO with septal collaterals from the right posterior descending coronary artery and a good distal target. (**b**) Successful antegrade crossing attempts using a CrossBoss catheter (Boston Scientific Corporation, USA) into the proximal cap of CTO. (**c**) Advance of the CrossBoss catheter through a subintimal space within the CTO. (**d**) Advance of the CrossBoss catheter to the re-entry point and change to a Miracle 12 wire (Asahi Intecc, Japan). (**e**) Successful antegrade crossing using a Stingray system (Boston Scientific Corporation, USA). (**f**) Final angiographic result after a 3.0 × 38 mm, and a 3.5 × 33 mm everolimus eluting stents implantation

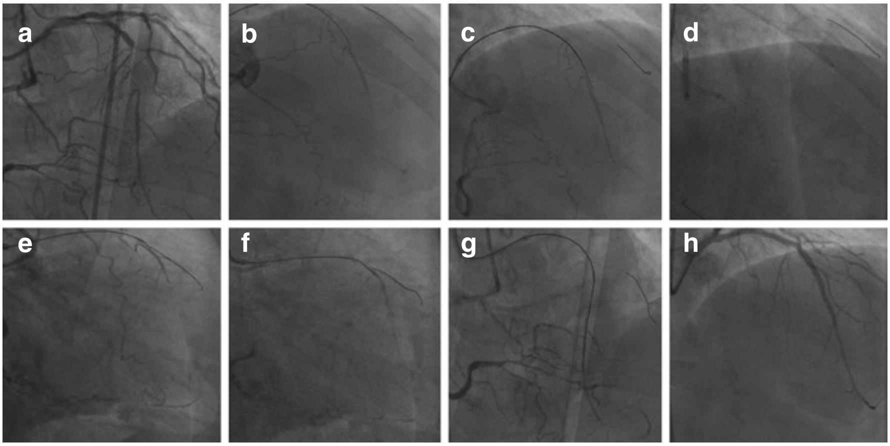


Fig. 9.4 Antegrade approach using ADR technique in recanalization of LAD CTO. (**a**) Bilateral coronary angiography demonstrating a mid-LAD CTO with septal collaterals from the right posterior descending coronary artery and a good distal target. (**b**) A Gaia second wire (Asahi Intecc, Japan) used for proximal cap puncture under the support of KDLC (Kaneka Corporation) via a Sion wire (Asahi Intecc, Japan) to the diagonal branch. (**c**) Failure of antegrade wire escalation technique with a Miracle 12 wire (Asahi Intecc, Japan) in the subintima. (**d**) Antegrade crossing attempts using a Stingray system (Boston Scientific Corporation, USA). (**e**) A Gaia third wire (Asahi Intecc, Japan) used for repeated antegrade crossing attempts. (**f**) Successful antegrade crossing attempts with the Gaia third wire. (**g**) The Gaia third wire in the true lumen confirmed by contralateral angiography. (**h**) Final angiographic result after a 2.75 × 38 mm, and a 3.5 × 33 mm everolimus eluting stents implantation

guiding catheter extension catheters (such as the Guidezilla catheter, Boston Scientific, Natick, Massachusetts, USA and the GuideLiner catheter, Vascular Solutions, Minneapolis, Minnesota, USA). A side branch anchor balloon provides more force than a coaxial guiding catheter extension catheter in the majority of cases, especially if the side branch is near the proximal cap of the CTO. The use of Tornus (Asahi Intecc) or Turnpike® Gold catheters (Vascular Solutions, Minneapolis, MN, USA) with side branch balloon anchor or coaxial guiding catheter extension catheter should be tried next. As for lesions that cannot be dilated by balloons, Tornus catheter, excimer laser, and coronary rotablation can be adopted.

9.5.2 Retrograde Technique of CTO PCI

9.5.2.1 Selection of Collateral Channels

Successful collateral crossing depends on the selection of collateral channels, wire tip curve, and wire handling, while careful analysis of the collateral channels with frame-by-frame study was the basis for collateral channel selection. The best collateral channel would be clearly visible, less tortuous collaterals by super-selective injection, exemplified by Dr. Werner's CC grade 1 or 2 (CCs are graded as follows: CC0, no continuous connection, CC1, continuous thread-like connection; and CC2, continuous, small SB-like connection) [22]. Usually, septal branches are the first choice of retrograde strategy. Well-developed epicardial collateral channels can be used with caution. The great saphenous vein bypass graft can also be used for part of the patients who had undergone the coronary artery bypass grafting (CABG). Severe lesions in the donor artery should be treated first to prevent donor artery thrombosis. Intermediate lesions in the donor artery may also cause ischemia or thrombosis, some of which should also be treated before commencing the retrograde approach.

9.5.2.2 Crossing of Collateral Channels

Guidewires with soft head end, good tactile feedback, and torque transmission should be used in crossing collateral channels. The main advantage of dedicated channel wires is that they can be controlled to rotate with one-to-one torque transmission allowing accurate wiring of the channel. The representative guidewire is Sion (ASAHI INTECC CO., LTD.). This guidewire can be advanced smoothly and safely because of its coated tip and 0.7-g tip load. When the collateral vessels are severely tortured and Sion guidewire cannot pass through, we can try Sion Black (ASAHI INTECC CO., LTD.) in big collateral channels, and try Fielder XT-R (ASAHI INTECC CO., LTD.) in tiny collateral channels with caution to prevent entering invisible vessels. Sion Black guidewire has features of polymer jacket and slip coating with rope coil structure of tip, which make better sliding in collateral channels, and can be advanced more smoothly and consequently. Fielder XTR guidewire has a polymer jacket coating with a 0.010 in. tapered tip. For collateral channels that are extremely tortuous (instant noodles like collateral channels), SUOH 03 is recommended. The SUOH 03 has a 0.3 g weight tip and a very flexible distal end, allowing it to find its own way through very tortuous channels. The SUOH 03, if available, should be the first-line wire to use in epicardial collaterals. After entering collateral vessel, guidewire should be shaped with an extremely small (<1 mm) curve, and large-angled tip bend from 70° to 90° for collateral channel tracking. When crossing collateral channels, the guidewire should be rotated. Do not push hard to cause collateral channels injury. For some collaterals of septal channels, surfing technique can be used for crossing the wire, but forbidden in epicardial channels [23]. SION or Fielder XT-R wires are recommended for channel surfing. In order to prevent injury of collateral channels, the guidewire should be manipulated under the guidance of selective injection. It is advisable to aspirate blood from the microcatheter before selective injection to minimize the chance of channel damage. If we fail to aspirate blood, we should move the microcatheter back and retry aspiration.

9.5.2.3 Microcatheter in Collateral Channel Tracking

Microcatheters with length of 150 cm should routinely be used in conjunction with the guidewire as part of collateral channel tracking, which allow for rapid exchange of guidewires and improve guidewires torque response. 90 cm guide catheter should be used for some cases with long traveling distance of collateral channels. Microcatheters improve support and allow the ability of guidewire tracking to be altered by changing the distance between the microcatheter tip and wire tip. Guidewire crossing of collateral channels can be facilitated by supporting of dedicated microcatheters (such as the Corsair, Caravel [Asahi Intecc, Aichi, Japan], and Turnpike [Vascular Solutions, MN, Minnesota], Finecross [Terumo, Japan]), which is safer than a balloon and rarely causes collateral channels dissection or perforation even with excessive tortuosity. Corsair microcatheter has a soft tapered tip with tungsten braiding and a hydrophilic shaft which serves as a collateral channel dilator while providing exceptional collateral channel tracking and crossing as well as retrograde wire control. Caravel is a versatile microcatheter with braided shaft providing flexibility and an excellent crossing profile (1.9 Fr) which tracks very well through tiny tortuous septal collateral channels without requiring rotation. This catheter technology has been revolutionary and transformative for safe, effective, and predictable retrograde procedures. If the microcatheter cannot pass the collateral channels along the wire, small diameter monorail balloon with low pressure dilation can be used in septal collateral channels but forbidden in epicardial collateral channels. If none of the above methods worked, it is recommended to change to other collateral channels timely, or to try antegrade strategy under the guidance of retrograde guidewires.

9.5.2.4 Handling of Collateral Channels Injury

Many septal collateral channels ruptures are benign and do not lead to adverse consequences, although septal hematomas [24] and even cardiac tamponade [25] have been reported. Septal collateral channels perforations usually do not require further treatment apart from abandoning that collateral channel and trying for another. For some patients, large hematoma or perforation of the septal collateral channels may lead to hemodynamic instability, and the embolization and symptomatic treatment shall be performed immediately. Perforation into cardiac chamber usually does not result in complications; however, balloon dilation or advancement of additional device should be avoided [26]. Epicardial collateral channels perforation can rapidly lead to cardiac tamponade and may be difficult to handle with, which should be treated actively and timely. Epicardial collateral channels should never be dilated to minimize the risk of perforation. Embolization should be performed both from the donor side and from the target vessel when occlusive lesions have been opened. In some cases of collateral channels injury, long-time negative pressure suction through a microcatheter can work effectively sometimes.

9.5.2.5 Retrograde Guidewire Technique

After the retrograde guidewire has crossed the collateral channels and reached the lumen of the coronary artery distal to the occlusion lesions, the following four strategies are available: direct retrograde wiring technique; kissing wire technique; controlled antegrade and retrograde tracking (CART) technique; and reverse CART technique [27, 28].

Direct retrograde wiring technique and kissing wire technique are mainly applicable to cases with shorter length of occlusion. If failed, it is recommended to use reverse CART technique as soon as possible. If the occluded segment is long and tortuous, or the expected occluded segment has complex anatomical structures and the success rates of direct retrograde wiring technique and kissing wire technique are low, it is suggested to carry out reverse CART technique as early as possible to improve the efficiency and success rate. The steps of reverse CART include retrograde dissection creating subintimal space past the distal cap, navigation of retrograde microcatheter over the dissection to near the proximal cap, antegrade dissection with subintimal space to a point distal to the retrograde microcatheter, and deployment of an antegrade balloon in the subintimal space next to the retrograde microcatheter with subsequent connection of both the subintimal space (common space) followed by retrograde wiring from the microcatheter into the proximal true lumen (Fig. 9.5). Conventional guidewire technique might result in perforation in extremely tortuous and calcified lesions, when Knuckle technique should be used when necessary.

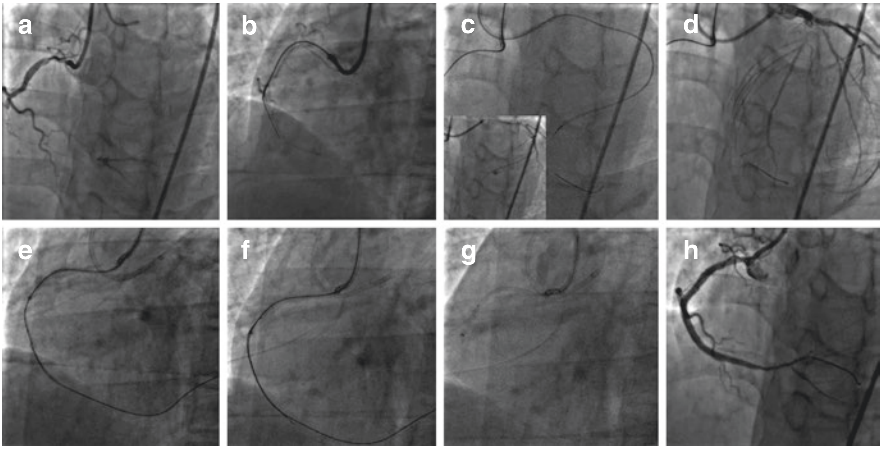


Fig. 9.5 Retrograde approach with reverse CART technique in recanalization of RCA CTO. (**a**) Proximal right coronary artery (RCA) CTO with tapered stump. Contralateral injection revealing retrograde filling of the distal vessel via epicardial collaterals. (**b**) Antegrade wire escalation technique failed with try of a Fielder XT-R wire (Asahi Intecc, Japan), a Fielder XT-A wire (Asahi Intecc, Japan), a Gaia 1 first wire (Asahi Intecc, Japan), and a Gaia 2 second wire (Asahi Intecc, Japan). (**c**) Conversion to retrograde approach with try of a Sion wire (Asahi Intecc, Japan) to cross the septal channels under the support of a Corsair microcatheter (Asahi Intecc, Japan). Failure of the Corsair microcatheter to cross the septal collaterals and injury of perforation of the septal collaterals. (**d**) Conversion to try of a Finecross microcatheter (Terumo, Japan) to advance into the distal true lumen over the Sion wire. (**e**) Bilateral wiring of the occlusion with a Gaia second wire antegrade and a Gaia third wire (Asahi Intecc, Japan) retrograde, supported by Corsair and Finecross microcatheters, respectively. A 2.0 × 15 mm antegrade balloon dilatations enlarging the subintimal space to facilitate retrograde wire crossing (reverse CART technique). (**f**) Guidezilla (Boston Scientific, USA) facilitated retrograde wire (Gaia third) crossing; the Finecross is advanced over the wire through the Guidezilla in the antegrade GC. (**g**) The externalization of an RG3 wire (Asahi Intecc, Japan) allows antegrade insertion of balloons and stents. (**h**) Final angiographic result after implantation of a 2.75 × 33 mm, a 3.0 × 33 mm, and a 3.5 × 38 mm everolimus eluting stents

When repeated attempts of reverse CART technique failed, we should consider the use of IVUS-guided reverse CART technique, stent reverse CART technique, mother-child reverse CART technique, contemporary reverse CART technique, confluent balloon reverse CART technique, and punctured antegrade balloon reverse CART technique.

Intravascular Ultrasound (IVUS), mother and child catheter [Guideliner (Vascular Solution, Minneapolis, MN, USA), Guidezilla (Boston Scientific, USA) or Guidion (IMDS, Netherlands)], and stent reverse CART techniques.

9.5.2.6 Externalization of the Guidewire

When it is difficult to advance the retrograde guidewire into the antegrade guide catheter, coaxial antegrade guide with guide catheter extension can be used to the target vessel, including Guideliner, Guidezilla, or mother-child catheter, also known as "Active Greeting Technique (AGT)" [29]. Despite coaxial antegrade guide, advance of retrograde wire into antegrade guide catheter fails in conditions such as aorto-ostial lesions or extremely tortuous vessels, or whenever there is poor retrograde wire control, when snaring technique can be used to scratch retrograde wire into antegrade guide catheter actively.

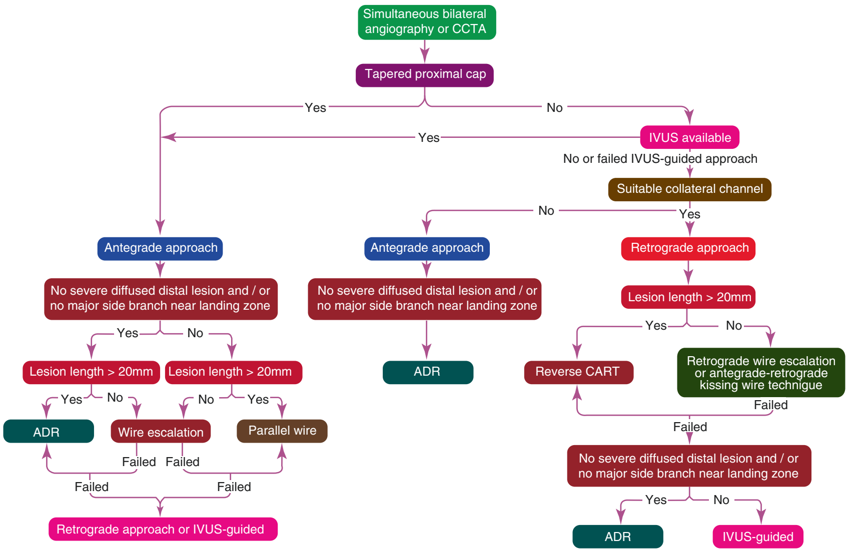
The crossing guidewire is changed for an externalization wire after a microcatheter is advanced into the antegrade guide catheter. The 330 cm RG3 (ASAHI INTECC CO., LTD.) guidewire is 0.010 in. tiny wire, considered and recommended as the most ideal guidewire for externalization at present. RG3 wire should be covered by microcatheters in segments of collateral channels in the process of interventions and when withdrawing RG3 guidewire to avoid the cutting effect by the guidewire. At the same time, ostial injury by retrograde guide catheter should be avoided. If RG3 wire is unavailable, other 300–330 cm wires can be used for substitute (but rotational ablation guidewire or extended guidewire should not be used). Rendezvous technique (microcatheter kissing technique) and its modified approach can also be used.

9.6 Summarized Roadmaps of CTO PCI Recommended [30] (Fig. 9.6)

Path 1: Antegrade strategy is recommended for CTO lesions with tapered stump as an initial strategy.

Path 2: In Path 1, in cases with good landing zone without major branches involved, ADR technique should be considered in case of length of occlusion more than 20 mm. Antegrade wire escalation strategy should be considered in case of length of occlusion less than 20 mm, and ADR technique could be attempted if antegrade wire escalation strategy failed (Figs. 9.3 and 9.4).

Path 3: In Path 1, in cases with poor landing zone or with major branches involved, parallel wiring technique should be attempted first in case of length of occlusion more than 20 mm (Fig. 9.1). Antegrade wire escalation strategy should be considered in case of length of occlusion less than 20 mm, and



CCTA: Coronary computed tomography angiography, ADR: Antegrade dessection re-entry, IVUS: Intravascular ultrasound, Reverse CART: Reverse controlled antegrade dissection re-entry technique,
CTO-PCI: Chronic total occlusion-percutaneous coronary intervention, CTOCC: Chronic Total Occlusion Club China

Fig. 9.6 Summarized roadmaps of percutaneous coronary intervention of chronic total occlusions

parallel wiring technique could be attempted if antegrade wire escalation strategy failed.

Path 4: For cases failed in Path 1–3, retrograde strategy or IVUS-guided antegrade strategy is recommended.

Path 5: For CTO lesions without tapered stump, IVUS is recommended for guidance in Path 1–4 (Fig. 9.2).

Path 6: For CTO lesions without tapered stump, if IVUS is unavailable or failed in Path 5, antegrade strategy is recommended in case of no available collateral channels. ADR technique is recommended in cases with good landing zone without major branches involved.

Path 7: For CTO lesions without tapered stump, if IVUS is unavailable or failed in Path 5, retrograde strategy is recommended in case of available collateral channels.

Path 8: For CTO lesions with length of more than 20 mm in Path 7, reverse CART is recommended first in retrograde strategy. Direct retrograde wiring technique or kissing wire technique is recommended first in case of length of occlusion less than 20 mm. If failed, reverse CART can be attempted (Fig. 9.5).

Path 9: For CTO lesions failed in Path 8, ADR technique is recommended in cases with good landing zone without major branches involved, and IVUS-guided antegrade strategy is recommended in cases with poor landing zone or with major branches involved.

In general, developments of instrument and technology in the area of CTO PCI have led to significant improvement in success rates of CTO PCI. But further improvements are heavily dependent on expansion of CTO PCI knowledge and education. These algorithm approaches in CTO PCI can provide a useful working and training framework for operators performing CTO PCI and may help increase attempt and success rates, improve efficiency, and minimize complications.

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CTO PCI Complications: Prevention and Management

10

Kohei Asada and Fumitaka Hosaka

In this chapter we perform a review of complications that may occur during CTO PCI. Over the past few years, tremendous improvement in PCI devices, as well as growth of new strategies has enabled us to treat with success even complex CTO. As CTO PCI is a complex procedure, it is associated with higher risk for complications as compared with PCI of non-CTO lesions [1]. Therefore it is critical to understand the potential complications with procedures, and steps that could be taken for mitigating risk. Patient-specific risk estimates can be calculated by using a dedicated scoring system, such as the PROGRESS-CTO complications score that uses 3 variables (age ≧65 years, lesion length >23 mm, and application of retrograde approach) [2]. Ellis et al. [3] reported the following 2 independent correlates of complications: moderate to severe lesion calcium and low left ventricular ejection fraction.

10.1 The Frequency of Adverse Events with CTO PCI

Rates of inpatient mortality and MACE from a single-center series of 25 years of CTO PCI has, reassuringly, suggested success rates are increasing, while adverse events are declining over time [4]. A systematic review by Patel and colleagues of 65 studies with 18,061 patients and 18,941 target CTO vessels revealed low risk for death (0.2%), emergent coronary bypass graft (0.1%), stroke (0.01%), MI (2.5%), and contrast nephropathy (3.8%) [5]. Perforation was reported at 2.9% with cardiac tamponade in 0.3%. An analysis of 2596 target CTO lesions from Japanese

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Table 10.1 Frequency of complications on CTO PCI

Mortality	0.2%
Myocardial infarction	1.2%
Stroke	0.2%
Emergent coronary artery bypass graft surgery	0.0%
Coronary embolism	0.2%
Coronary perforation (tamponade)	0.4%
Vascular access complications	1.3%
Contrast induced nephropathy	1.7%
Radiation skin injury	0.2%

CTO-PCI Expert Registry revealed the complications consistent with above-mentioned study (Table 10.1) [6].

Regardless of the small numbers of serious complications, CTO operators should be aware of these events and should be able to treat them immediately if needed.

10.2 General CTO PCI Complications

10.2.1 Perforation

Coronary perforation is a well-known complication of CTO PCI. It is one of the most feared complications of CTO PCI which can lead to cardiac tamponade necessitating emergency pericardiocentesis and rarely, cardiac surgery to be controlled. It could be caused directly by the guidewire or by subsequent balloon advancement and dilatation. To avoid complications, balloon advancement or dilatation and microcatheter advancement should not be performed when the guidewire is not confirmed to be within the vessel. It is also important to size balloons appropriately using intravascular ultrasound (IVUS) and pay careful attention to tip hydrophilic or polymer-jacketed wire during attempts to delivery devices.

Coronary perforations are categorized according to location. There are three main perforation locations: large vessel perforation, distal artery perforation, and collateral vessel perforation, in either a septal or an epicardial collateral [7]. And the severity of coronary perforations has traditionally been classified according to the Ellis Criteria (Table 10.2) [8]. The general treatment of coronary perforations is shown in Fig. 10.1 [9] and the first step in any coronary perforation is inflation of a balloon to prevent additional bleeding into the pericardium. If there is a significant bleed while working with a 6Fr or 7Fr guide catheter, it is often useful to site a second guide catheter in the same vessel (a dual guide technique). However, a dual guide technique is not required if a 8Fr guide is used when covered stent delivery and continued balloon inflation can be managed via a single guide.

10.2.1.1 Coronary Perforation by Guidewire

Coronary perforation by a guidewire is the most frequent complication of CTO PCI. Guidewires for CTO have stronger penetrability than conventional guidewires; namely, some have a hard tip, some are tapered, and some are coated. Since the lesions are complex, the risk of perforation of the coronary arteries is high.

Table 10.2 Ellis criteria of coronary perforations

Perforation type	Description
Type I	Extraluminal crater without myocardial brush, extravasation or evidence of dissection
Type II	Myocardial or pericardial blush without extravasation
Type III	Extravasation through a ≥1 mm perforation
Type III: cavity spilling	Perforation and extravasation into an anatomic cavity chamber

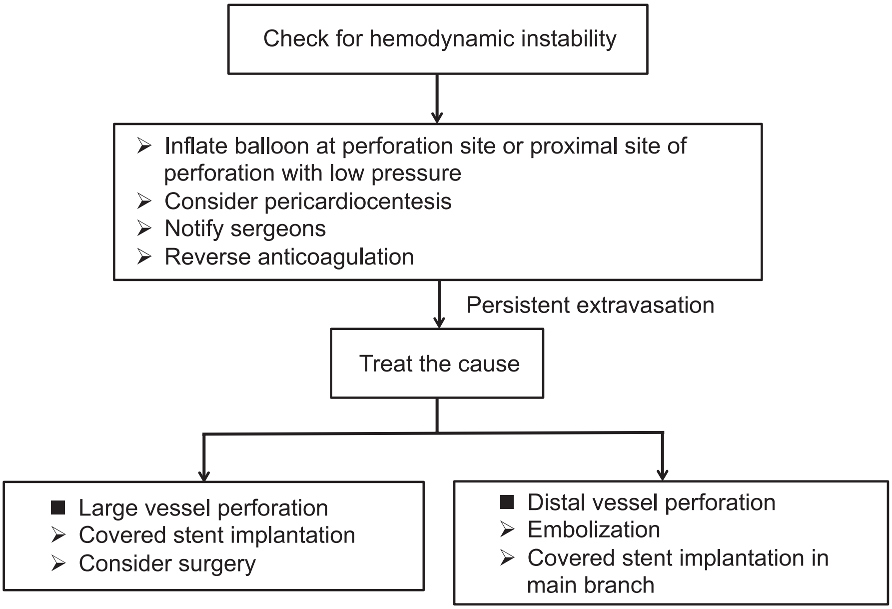

Fig. 10.1 Perforation management algorithm

Most of the time, operating a guidewire inside a CTO lesion is similar to relying on finger touch with only a vague image of the path of the coronary arteries. In perforations originating from inside a CTO lesion, blood is absent at the lesion and the plaque itself forms at the perforation site; as a result, blood rarely leaks from the blood vessel.

If coronary perforation occurs after the guidewire reaches the distal coronary arteries, it will be complicated by bleeding, which may be difficult to control. In situations in which a guidewire successfully passes through the lesion but the device has difficulty passing through it, moving the guidewire back and forth may cause coronary perforation during the procedure. In perforations occurring before the passage of the device through the CTO lesion, blood is supplied to the distal coronary arteries from the collateral circulation; therefore, perfusion pressure is low and only mild blood leakage results. However, even if the blood leak is mild, it may cause cardiac tamponade; thus, dilatation should be performed as quickly as possible at the CTO site, and proper hemostatic treatment is required as soon as possible.

Hemostatic interventions include pressure using a balloon, occlusion by a microcatheter, and embolization using thrombi, adipose tissue, or coil when appropriate, but coil embolization infallibly stops the bleeding.

A particularly serious issue is when the guidewire causes perforation of the distal coronary arteries before dilatation of the CTO lesion, making it impossible for the device to pass through the CTO lesion and causing hemodynamic failure due to cardiac tamponade. In such situations, hemostasis devices cannot be placed; therefore, hemodynamics must be maintained through vasopressor administration and pericardial drainage. In some cases, hemostasis through thoracotomy may also be needed. After hemodynamics are stabilized through procedures such as pericardial drainage, attempts can be made to pass the device through the CTO lesion while continuing observation, but if the effect of heparin is reversed, caution must be taken against thrombus formation.

Because perforation due to a guidewire is often asymptomatic in the period immediately following its occurrence; as a result, it may remain unnoticed during the procedure and left untreated once the patient is returned to their hospital bed. However, several hours later, the patient may suddenly develop a decrease in blood pressure, and perforation is only discovered after the patient develops cardiac tamponade. This is why the entire coronary artery that was subjected to revascularization must be subjected to angiography after the procedure. Confirming the absence of perforation due to the guidewire is of crucial importance.

10.2.1.2 Coronary Perforation by Balloon Dilatation

One way to help the guidewire pass through the CTO lesion is by introducing a microcatheter or intravascular ultrasonography (IVUS) into the CTO lesion before letting the guidewire pass through it. In such cases, the proximal site inside the CTO lesion is dilated using a small-diameter balloon; it has not been determined whether the tip of the guidewire is inside or outside the coronary artery. Although the balloon has a small diameter, a massive hemorrhage could occur if the balloon is inflated outside the coronary artery. As a countermeasure, one must stop the bleeding by re-inflating the balloon. Later, another guidewire is inserted inside the CTO lesion via another route or using the retrograde approach, the balloon is inflated, and hemostasis is achieved by compression of the plaque inside the CTO lesion at the site of the rupture; this makes hemostasis possible but requires tremendous skills and experience. First, efforts should be made to stop the bleeding and achieve hemodynamic stability. It is most important to carefully examine the benefits and risks associated with balloon inflation before passing the guidewire through the lesion.

10.2.2 Side Branch Occlusion

In most cases, CTO lesions start forming anteriorly and posteriorly to the site of the occlusion and ramify into the side branches. Most patients with CTO lesions also have cardiac dysfunction, and troubles commonly involve the side branches, leading to severe complications. If the side branches diverge from the proximal portion of the occlusion, the guidewire must be inserted into side branches to prepare for unforeseen occlusions of the side branches and other troubles.

Further, the distal end of the occlusion in the CTO lesion often consists of bifurcation of the lateral branch. When the guidewire is pushed forward from inside the CTO lesion and penetrates the distal coronary arteries, effort should be made so that penetration occurs from the apex of the distal end of the occlusion. After the guidewire passes through the lesion, the CTO lesion is dilated using a small-diameter balloon; later, the remaining branches must be immediately secured using a double-lumen catheter. The situation that must be avoided the most is one in which the guidewire shortcuts the bifurcation and directly perforates either of the branches.

10.2.3 Coronary Dissection or Hematoma

Even if the guidewire successfully reaches the distal coronary arteries, dissection and hematoma formation can occur during the guidewire progression. This can go unnoticed, and angiography after balloon dilatation may reveal a dissection or hematoma that may have progressed to the distal. As a countermeasure, angiography should not be performed after balloon dilatation; instead, IVUS is first performed to confirm the presence of a dissection or hematoma, and later, indwelling stent placement should be performed under IVUS guidance.

10.3 Complications of the Retrograde Approach

The success rate of CTO PCI has improved due to the widespread use of the retrograde approach. In addition, suitable devices have been developed and its safety has improved; however, the retrograde approach has its own specific complications, most of which are likely to be fatal. This must be considered during the procedure.

10.3.1 Complications of Coronary Artery with CTO

10.3.1.1 Advance of Coronary Dissection or Hematoma

The reverse controlled anterograde and retrograde subintimal tracking (CART) method is currently the mainstream method in the retrograde approach. In this procedure, the condition is that the CTO lesion should be dilated before the guidewire reaches the distal coronary arteries. The space that was dilated by the antegrade balloon will expand as a dissection if it is inside the intima or as a hematoma if it is inside the subintima. If antegrade contrast injections are performed after antegrade balloon dilatation, it may cause the dissection and hematoma to extend more distally, giving rise to complications such as occlusion of the distal coronary arteries. This is why—in principle—antegrade contrast injections must not be performed under such circumstances. Even if antegrade contrast injections are not performed, the dissection and hematoma may still extend through antegrade coronary blood flow, but there is no need to worry about such a risk as long as the antegrade balloon remains dilated during the procedure.

10.3.1.2 Proximal Coronary Injury by Retrograde Guidewire

The proximal end of the occlusion in a CTO lesion is often located at the bifurcation, and after a procedure consisting of making a retrograde guidewire pass directly inside a proximal coronary artery, IVUS must be performed for confirmation. In some cases, the retrograde guidewire may reach the proximal coronary artery by shortcutting the coronary bifurcation. If the operator fails to notice this and proceeds with the dilatation, the side branch on the proximal side could be obstructed; if this happens in patients with reduced cardiac function or large side branches, it may lead to lethal complications. If IVUS findings confirm shortcutting of the coronary bifurcation, switching to the reverse CART method inside the CTO lesion would be appropriate.

10.3.2 Collateral Channel Injury

When creating a system to perform the retrograde approach, one must first advance the guidewire and device to the distal coronary artery through the collateral channel. The pathways include the septal channel, epicardial channel, and bypass graft.

Damage to the collateral channel can be classified into two categories: damage due to the guidewire and damage due to the device. In terms of frequency, the more common types are guidewire-induced damage. Guidewire manipulation can obstruct the collateral channel, but in most cases, blood also flows in from other collateral channels; therefore, this issue is unlikely to cause any problems. Perforations due to the guidewire also often occur. When the damage involves the septal channel, the bleeding often penetrates the right and left ventricles as well as the coronary veins, rarely causing problems. However, guidewire-induced perforations in the epicardial channel can cause cardiac tamponade and hemodynamic collapse; therefore, the bleeding must be stopped through coil embolization or microcatheter occlusion. When bleeding occurs in the epicardial channel and the guidewire has already passed through the lesion, hemostasis should be achieved by pushing the microcatheter forward to block the blood flow, and the procedure has to be continued by using the retrograde approach. Finally, to confirm that the bleeding has stopped, angiography must be performed, while the retrograde guidewire is left in place; if the bleeding persists, bleeding from both the anterograde and retrograde directions must be stopped.

Damage to the collateral circulation due to passage of the device has become less common since devices have undergone improvements. The damage is often discovered after device removal; thus, when a retrograde device is removed, the guidewire must absolutely be left in place when angiography is performed, and the latter must be performed to confirm the presence or absence of bleeding or damage to the collateral circulation. If the damage affects the septal channel, a hematoma forms inside the myocardial septum, causing ischemia or ventricular arrhythmia; therefore, a shunt with the cardiac ventricles should be formed using another guidewire, and the pressure inside the hematoma must be reduced. If the damage affects the epicardial channel, it may lead to cardiac tamponade; therefore, the bleeding must be stopped immediately using coil embolization from the anterograde and retrograde directions. To ensure that hemostatic treatment can be performed in emergency situations, the operator should ensure that the coil they are familiar with is always ready to be used during PCI.

10.3.3 Donor Artery Injury

A donor artery injury often induces extensive ischemia and hemodynamic collapse. This is due to the guiding catheter, which injures the proximal portion of the donor coronary artery. In the retrograde approach, stronger than usual forces are applied to the guidewire and the device; as a result, the guiding catheter can easily be drawn deep into the coronary artery. Under such circumstances, it is likely to injure the proximal portion of the donor coronary artery. If stenosis occurs at the proximal site of the donor coronary artery, the retrograde approach should be preceded by the deployment of stent to avoid complications. If externalization is successfully achieved, the procedure should be continued while the guiding catheters on both sides are completely removed from the coronary artery.

10.3.4 Ischemic Phenomenon of Donor Artery

If a moderate or severe stenosis occurs in the donor coronary artery, the stenosis must absolutely be treated before the retrograde approach is started. If device passage induces ischemia, chest pain and hemodynamic instability will occur. Even if the clinical course is uneventful immediately after the device passage, ischemia can sometimes be induced by the maneuvering of a retrograde device or the induction of vasodilation and vasospasm; therefore, procedures such as stent deployment should absolutely be performed before use of the retrograde approach.

Even if a collateral channel with abundant blood flow is used as a route for the retrograde approach, ischemia that may be induced by the procedure does not normally pose any problems in most cases. Even if the collateral channel is occluded by the retrograde device, blood flowing from other collateral channels will increase and chest pain as well as electrocardiographic changes will be mild. However, when a collateral channel with direct communication is used as a route for the retrograde approach, the ischemia that is induced by the occlusion of collateral channels will be strong; even if the hemodynamics are maintained, a strategic change may be imperative in some cases.

10.3.5 Embolization

Thrombus formation is among the complications that require the most caution with the retrograde approach. During the retrograde approach, the procedure is often continued for long hours without angiography or device replacement while a guiding catheter is left inserted in the coronary arteries on both sides; as a result, the blood inside the guiding catheter may stagnate and a thrombus may form. If the resulting thrombus flows into the donor coronary artery, it may cause hemodynamic collapse and could lead to lethal complications.

As a preventive measure, the activated clotting time (ACT) should be controlled and constantly maintained at 300 s or higher during the procedure. Because heparin has a short half-life, its effect is attenuated during the procedure; therefore, in our facility, the ACT is measured every 30–60 min, and additional heparin doses are administered when appropriate. Further, during a procedure using the retrograde approach, flash injections of heparin sodium are administered every 30 min through the retrograde guiding catheter.

10.4 Conclusions

Since CTO PCI is believed to carry a higher incidence of complications than conventional PCI, it must be performed with consideration of preventive measures and countermeasures against all possible complications. It is important to know that, as a pathological condition, CTO is stable to some extent; even if the first treatment is unsuccessful, it can be replaced with PCI or other treatment strategies at a later date. Thus, making the decision to terminate the procedure instead of pushing too far is also crucial in cases of complications.

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Providing Education About PCI for CTO

11

Toshiya Muramatsu

11.1 Introduction

Performing PCI for CTO is the most technically difficult interventional procedure and gaining sufficient skill to treat CTO is often the final goal of interventionists. However, considerable effort over a long period (years to decades) is required to achieve this goal. When standard PCI is performed to treat stenosis, the course of the target vessel can be confirmed by angiography, but this is impossible during PCI for CTO. Since the target segment of the occluded vessel cannot be observed angiographically, it is necessary to manage an invisible lesion, so the course of the target vessel has to be predicted and treatment is provided depending on the experience, knowledge, and assumptions of the interventionist. Accordingly, good instructors are essential for educating interventionists about PCI for CTO and it is also desirable to develop a specific education program. In the past, many CTO interventionists have learned the relevant techniques from their own experience. At present, the number of CTO patients is limited and the number of interventionists is increasing, which makes it important to establish systematic methods for education and guidance regarding management of CTO in the future.

11.2 Required Level of Skill

∗The most important point in relation to improving the success rate of PCI for CTO is gaining experience with a large enough number of cases. As reported by the Euro CTO Club [1], the procedural success rate in JCTO 1–3 patients is ≥90% for interventionists who have treated more than 2500 CTO patients. In my experience, the

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success rate becomes higher and the complication rate declines along with an increase in the number of CTO cases, so the problem is how to obtain a sufficient number of cases. Recently, most hospitals have designated a single interventionist to treat all of the patients with CTO, which means that physician gains experience in PCI for such lesions. However, the result is that there tends to be only one interventionist per hospital who is skillful in handling CTO. In addition, both hospitals and interventionists have recently increased in number, so not all hospitals obtain a sufficient number of patients with CTO. Under these circumstances, how to train and foster interventionists specializing in PCI for CTO is an important issue.

11.3 Training Interventionists in Techniques for Management of CTO

∗In the current training process, a relatively simple CTO with a JCTO score of 1 is selected and the antegrade approach is initially attempted under the guidance of an experienced physician [2]. Based on the antegrade wire escalation method, treatment is started by using a tapered floppy guidewire, which is then stepped up to an intermediate weight wire or a stiff wire depending on the hardness of the lesion. If the guidewire enters a false lumen, the method is changed to the parallel wire technique. Further techniques must be learned, including those using IVUS guidance, and it takes several years to acquire this series of techniques. If the antegrade approach fails, the retrograde approach is tried next. However, mastering the retrograde approach requires more time than the antegrade approach, since it is necessary to learn various techniques and skills, including the indications for retrograde wiring, selection of a retrograde channel, and selection of wires and techniques. After the retrograde channel has been crossed successfully, it is also necessary for the interventionist to master the techniques for retrogradely crossing the CTO, such as direct wire crossing, the kissing wire technique, reverse CART technique, knuckle wire technique, and IVUS-guided methods [3].

It should not be forgotten that measures for prevention and treatment of complications related to these CTO procedures must also be learned. There are various CTO-specific complications and these occur at a higher incidence than complications of standard PCI. Therefore, the range of countermeasures for complications should be broadened simultaneously with improvement of procedural techniques.

Learning the required series of CTO techniques has generally been performed by direct guidance under an experienced physician in the catheter room. However, it is often quite difficult to give procedural guidance in the catheter room, especially when treating CTO by the retrograde approach, which is associated with great complexity. In the future, curriculum-based training programs and hands-on technical guidance will become essential parts of education in safer and higher-quality PCI for treatment of CTO.

11.4 Development of Training Programs

At present, education about the management of CTO is generally provided by lectures at meetings of academic societies, or by experienced interventionists who are invited to demonstrate their techniques through live demonstrations or lectures in catheter rooms. However, technical guidance about procedures is the most important point and this tends to be inadequate. Therefore, it is important to develop models that can be used for hands-on training of interventionists with respect to PCI for CTO. I would like to introduce several silicone vascular models that we use.

11.4.1 Antegrade 2D Wiring (Fig. 11.1)

When manipulating an antegrade guidewire, it is important to advance it while viewing the CTO from 2 directions because the wire can easily enter a false lumen if the CTO is only viewed from 1 direction. Bidirectional (frontal and lateral) wiring can be performed if cameras are installed to visualize the CTO in 2 directions.

11.4.2 Retrograde Channel Tracking (Fig. 11.2)

Training in retrograde channel tracking is performed by using a pulsatile model. An ordinary guidewire is inserted into the channel using a microcatheter and the channel is confirmed by tip injection. After that, the wire is replaced by a channel tracking guidewire and the channel is followed. After successful crossing with the guidewire, tracking the channel with a microcatheter is also attempted.

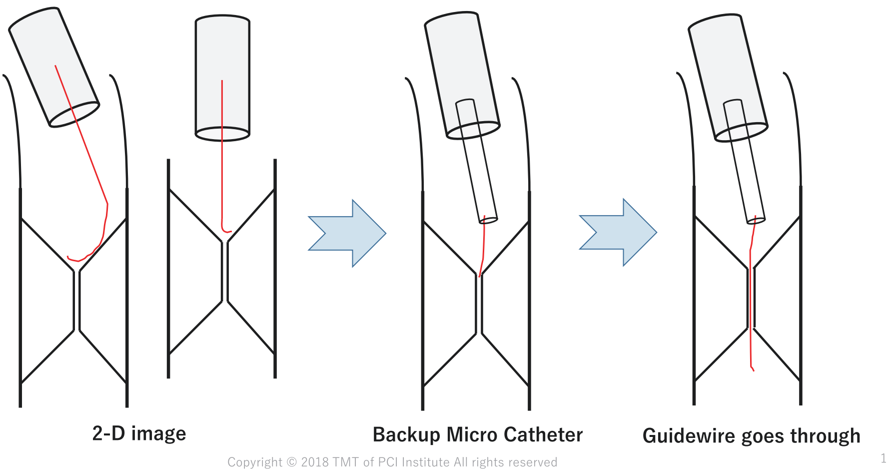


Fig. 11.1 Guidewire shaping and handling/microcatheter

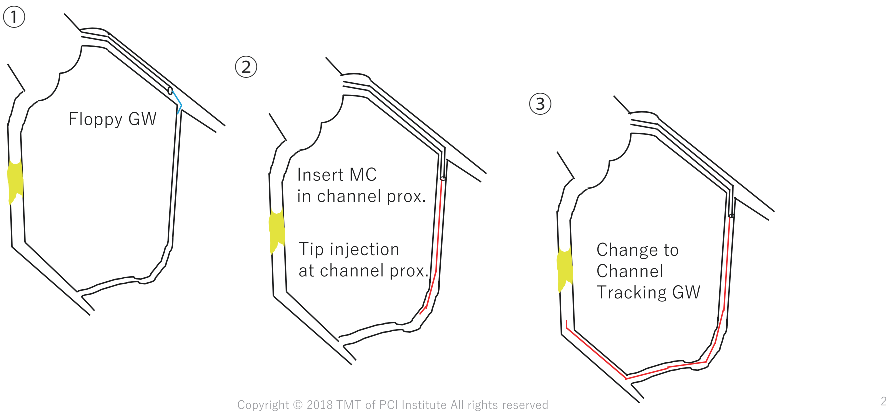


Fig. 11.2 Retrograde channel tracking

11.4.3 Retrograde Reverse CART (Fig. 11.3)

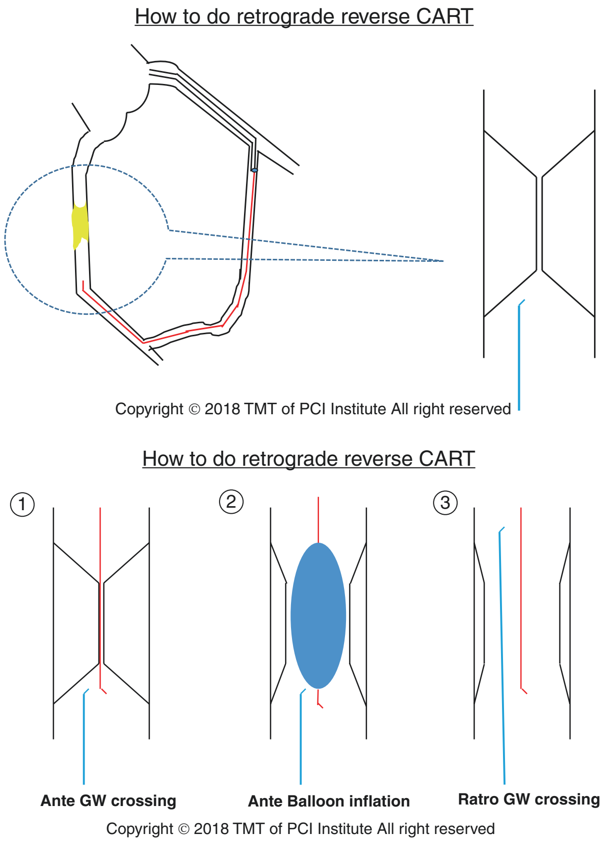
The retrograde approach to CTO by the reverse CART technique is also performed by using a pulsatile model. An antegrade guidewire is advanced partly through the CTO, after which it is crossed with a retrograde guidewire. Subsequently, the CTO is dilated with a 2.5-mm antegrade balloon and the retrograde guidewire is advanced through the CTO simultaneously with balloon deflation.

If several vascular models are used, training can be performed before actual manipulation of the wires and devices in clinical practice, allowing the processes of CTO wiring via the retrograde approach to be repeatedly practiced in stages. Thus, importance is not only attached to learning the theory, but also to actual hands-on training.

11.5 Conclusions

While it is obviously necessary for physicians to make efforts to learn the various techniques used in PCI for CTO, many other elements are also important, such as the hospital environment and mentoring physicians. Learning the techniques to manage CTO requires a long time, much patience, and continued enthusiasm. Recently, many talented young interventionists have entered the medical workforce. There is a growing demand for development of comprehensive and practical programs for guidance and education so that such enthusiastic young physicians can evolve into first-class interventionists without discouragement. In particular, more hands-on programs attaching importance to technical guidance are considered to be required in the future.

Fig. 11.3 Retrograde CTO crossing



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Future Prospects of PCI for CTO

12

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12.1 Introduction

Catheter procedures for the cardiovascular system have made rapid progress over a period of approximately 40 years since Dr. Grüntzig first performed percutaneous coronary balloon angioplasty in humans in 1977 [1]. Subsequently, the catheters and other devices have made rapid progress, along with catheterization techniques and application to the systemic vascular system.

12.2 Problems with PCI for CTO

PCI for CTO has been performed actively since the 1990s and is still considered to be the most difficult interventional treatment. After the development of specific guidewires for CTO, various methods such as the parallel wire technique, IVUS-guided procedures, and antegrade dissection re-entry technique were developed for treating CTO via the antegrade approach [2]. Thanks to development of dedicated guidewires and microcatheters, management of CTO via the retrograde approach has made rapid progress from the early 2000s, leading to various innovations such as the reverse CART technique, IVUS-guided procedures, and the knuckle wire, guide extension, and externalization techniques [3]. Owing to these various advances, the PCI strategy for CTO has now been almost completely established, but there are still some problems that need to be solved.

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12.3 Future of PCI for CTO

Currently, the early success rate of PCI for CTO is over 90% [4]. On the other hand, there are still some patients in whom this procedure is unsuccessful, as discussed next.

12.3.1 Patients with Calcified Lesions

CTO associated with severe calcification cannot be treated easily by either the antegrade or retrograde approach. While a Rotablator can be helpful, using this device is impossible without first successfully tracking the CTO with a guidewire and a microcatheter. Even when the retrograde reverse CART technique is used, it is not easy to form a subintimal space outside a heavily calcified lesion. The problems caused by calcification could potentially be solved by development of new devices, such as those for laser and shockwave therapy [5].

12.3.2 Patients Without Crossable Channels

PCI becomes very difficult if the antegrade approach fails and there are no appropriate channels for retrograde tracking. The antegrade dissection re-entry technique may be effective in some cases, but it is often difficult to employ in patients who have already undergone antegrade IVUS-guided intervention. Because there will continue to be limitations on channel tracking in some patients, it is hoped that devices with both imaging and CT guidewire functions can be developed for them [6].

12.3.3 Patients Indicated for CABG

Whether PCI is more effective than CABG for certain lesions, including CTO, is still controversial with respect to the cost, success rate, and long-term outcomes. We consider that PCI is not indicated for CTO patients who can be treated by CABG, except when the invasiveness will be much lower and the success rate is expected to be nearly 100% [7].

12.3.4 Level of Invasiveness

It is important to minimize the burden on patients, including the extent of exposure to radiation and the dosage of contrast medium. The level of invasiveness should also be reduced by the use of the transradial approach, etc. Without these efforts, consensus about the position of PCI for CTO will not be achieved in the future.

12.3.5 Indications for PCI and Long-Term Outcomes

No definite conclusions have been obtained concerning the CTO patients for whom PCI is more effective, and this question is also related to determining the indications for PCI. According to recent randomized studies, the long-term outcome of CTO shows no difference between PCI and drug therapy. In other words, it has not been clarified how candidate patients should be selected and what endpoints should be used. It is necessary to demonstrate good long-term outcomes of PCI for CTO located in major coronary arteries such as the proximal RCA and LAD [8].

12.3.6 Training for CTO Specialists

The most urgent issue is training for specialist CTO interventionists. Up to now, there have been no specific training programs for CTO interventionists. In other words, physicians had to study and train themselves in order to master the required skills [9]. However, it requires a long time to obtain sufficient experience with this method of learning. Because PCI is now a very common procedure, it is difficult for an interventionist to bear the heavy burden of working and studying simultaneously. In the future, it will be essential to develop study curriculums, training programs, and training courses for CTO interventionists. It is also important to improve the medical environment, including infrastructure and software, so that interventionists can obtain experience of more difficult cases.

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