How to Recanalize In-Stent Chronic Total Occlusions

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Benjamin Faurie and Stéphane Rinfret

Abstract

In-stent chronic total occlusions (IS CTOs) remain one of the most difficult and challenging subset of lesions in the field of CTO interventions. In a modern practice, this is not a rare situation and the prevalence has been reported between 5 and 25 % of all CTOs. Given that patients with CTOs caused by in-stent restenosis (ISR) are usually excluded from clinical trials, little published data exists to guide coronary intervention in this setting.

The clinical impact of IS CTO is fairly significant and most patients will present with recurrent stable angina at the time of repeat angiography (60 %), while a minority of these patients present with unstable syndrome.

These procedures have traditionally been associated with low success rate mainly due to wire crossing difficulties. The pathophysiology of these specific occlusions is perceived by CTO operators to play a role in the behavior of wires and subsequent success. In this chapter, we will discuss the specificities that makes in-stent occlusions challenging to re-open. Then, we will discuss how angiographic appearance can guide our strategies and how the hybrid algorithm apply to this specific entity. Finally, we will discuss different bailout techniques to avoid failing the intervention.

Keywords

In-stent chronic total occlusion (IS CTO) • In-stent restenosis (ISR) • Hybrid algorithm • Prevalence of CTO due to ISR • In-stent occlusive restenosis

Introduction

In-stent chronic total occlusions (IS CTOs) remain one of the most difficult and challenging subset of lesions in the field of CTO interventions. In a modern practice, this is not a rare situation and the prevalence has been reported between 5 and 25 % of all CTOs [1–4]. Given that patients with chronic total occlusions (CTOs) caused by in-stent restenosis (ISR) are usually excluded from clinical trials, little published data exists to guide coronary intervention in this setting.

The clinical impact of IS CTO is fairly significant and most patients will present with recurrent stable angina at the time of repeat angiography (60 %), while a minority of these patients present with unstable syndrome [5].

These procedures have traditionally been associated with low success rate [2, 3] mainly due to wire crossing difficulties. The pathophysiology of these specific occlusions is perceived by CTO operators to play a role in the behavior of wires and subsequent success. In this chapter, we will discuss the specificities that make in-stent occlusions

B. Faurie, MD (✉)
Institut Cardiovasculaire, Groupe Hospitalier Mutualiste de Grenoble, Grenoble, France
e-mail: b.faurie@ghm-grenoble.fr

S. Rinfret, MD, SM
Multidisciplinary Department of Cardiology, Quebec Heart and Lung Institute, Quebec City, QC, Canada

Laval University, Quebec City, QC, Canada

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challenging to recanalize. We will further discuss how angiographic appearance can guide our strategies and how the hybrid algorithm applies to this specific entity. Finally, we will discuss different bailout techniques to optimize the intervention whilst minimizing failure rates.

Prevalence

The prevalence of CTO due to ISR was 10.9 % in the Christopoulos et al. registry [1]. In a study of 78 patients, Abbas et al. reported a 25 % prevalence of CTOs due to ISR [2], whereas Wilson et al. reported a 14.9 % prevalence of ISR in 349 CTO PCIs [4]. Following literature and personal database review, Werner et al. estimated that 5–10 % of all CTOs were due to ISR [3]. However, the true incidence of in-stent occlusion following PCI remains largely unknown. While Shah et al. reported a 1.6 % rate of bare metal stent total occlusion in 955 native coronary lesions at 6-month angiographic follow-up [5], the occlusion rates following DES are much lower.

What Is Unique to In-Stent Occlusions?

First of all, in-stent CTO can be a consequence of in-stent restenosis (ISR) or stent thrombosis (ST). The proportion of these two entities remains unknown although stent thrombosis is probably less frequent due to a clinical presentation that tends to be more often acute than chronic. In addition to a large tissue burden, there will be, after successful crossing of an IS CTO, at least two layers of stent struts, resulting in higher stent recoil and the need for higher inflation and post dilatation pressures with adequately sized balloons. To counteract the expected higher lesion recurrence, one needs to consider the adverse synergistic consequences of a CTO ISR lesion. Therefore, optimal stent apposition and expansion is required, which can be best achieved by intravascular ultrasound guidance. This may, then, also minimize the potentially higher late stent thrombosis risk resulting from multi-stent layers [3].

Pathophysiology

In-Stent Occlusive Restenosis

As for other types of in-stent restenosis, those resulting in complete vessel occlusion may result from stent recoil, underdeployment or fracture that lead to smooth muscle cells ingrowth (neointima proliferation). This phenomenon was frequent with BMS but dramatically decreased with drug eluting stents (DES). Christopoulos et al. [1] underlined the role of diabetes mellitus for in-stent restenotic CTO genesis. Diabetes was present in 56.1 % and 39.6 % ($p=0.02$) respectively for in-stent CTOs and de novo CTOs. The other differences between the two groups were the occlusion length which was greater in the in-stent CTO group: (38 mm (29–55) vs. 30 mm (20–51), $P=0.04$) and the calcifications were less important than the de novo CTO group: 5.3 % vs. 16.2 %, $P<0.001$. Indeed, CTOs that result from in-stent restenosis are most commonly composed of a hypocellular matrix made up primarily of hard and resistant collagenous material, and therefore differ from other CTOs because of a relative absence of in-plaque microchannels, thus explaining the lower success rates evident with soft, tapered wires [6]. However, in some cases, the restenosis process is spotty and leave some areas of patent “islands” within the stent, likely highlighting a different proliferative process. In some cases, it is presumed that the restenosis process was concentric, therefore leaving a central area of looser tissue in the centre of the occluded stents. Penetrative wires with high tip loads are sometimes required in this setting but often result in wire passage through the stent struts, precluding subsequent device delivery, even if the distal true lumen has finally been successfully wired.

In-Stent CTO as a Result of Previous Thrombosis

As said, there are two pathophysiological mechanisms proposed stimulating for the occurrence of CTOs following stent implantation; neo-intimal proliferation; acute thrombosis leading to an organized CTO, or a mixture of both. Some stents are occluded likely as a result of a previous stent thrombosis, a condition that was more likely to occur with the earlier DES generations, and when mechanical factors such as poor expansion, distal dissection and poor outflow were overlooked when the stent was first placed. The proportion of in-stent occlusion that result from an earlier thrombosis is however unknown.

Angiographic Appearance of In-Stent CTOs

Usual angiographic predictors of successful percutaneous coronary intervention (PCI) for de novo CTOs play a limited role in patients who have IS CTO, and the mechanisms of failure are different.

IS CTOs can have different angiographic appearance depending on the restenosis or thrombotic phenomenon and time of occlusion. When the CTO results from a restenotic process, the proximal cap tends to be more frequently tapered than if a previous thrombosis caused the occlusion (Fig. 10.1). These will frequently present with in-stent patent lumen islands that interrupt the occlusion length. But overall, in-stent occlusions are more frequently blunt at the proximal cap compared with de novo CTOs [2]. Sometimes, a microchannel is visible in portion of the stent occlusion especially

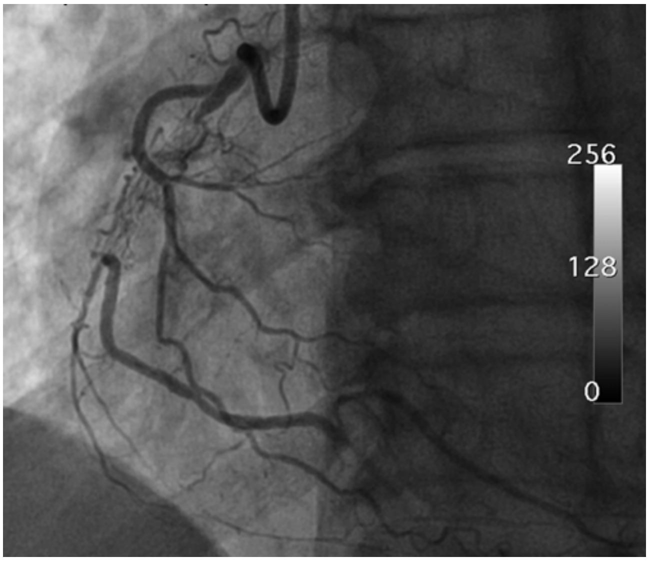

Fig. 10.1 IS CTO due to restenosis with a tapered proximal cap

when islands of patent coronary artery are present. This aspect suggest restenosis as the most likely mechanism and is easier to cross with CrossBoss (CB) catheter (Figs. 10.1 and 10.2).

On the other hand, in-stent chronic thrombosis are more likely associated with poor initial angiographic results with residual dissections or heavy disease at the proximal or distal edge of the stent. They often are associated with completely occluded stents, showing no patent islands, with the proximal cap starting proximal to the entrance of the stent (Fig. 10.3). The original post PCI result can actually give an idea as to why the stent occluded in the first place. If a perfect result was documented, and the patient presents with progressive symptoms, a restenotic process was the most likely the culprit phenomenon. However, if stents were placed as a result of dissections, if poor outflow was present at the end of the procedure, thrombosis might have occurred, especially when considering an angiographic appearance such as depicted in Fig. 10.3.

Treatment Algorithm Applied to This Entity

Low success rates with conventional antegrade wire-based approach even in very skillful and experienced hands have been reported. There is limited published data on the success of IS CTO PCI. Werner et al. reported a 70 % primary success in IS CTOs compared to 85 % in de novo lesions [3]. Abbas et al. reported 63 % procedural success in patients with CTOs due to IS restenosis [2]. These lower success rates occur despite the presence of previously placed stents serving as a "road map" of the course of the occluded artery as well as providing some protection against vessel perforation. Failure usually results from the inability to cross the lesion with a guidewire, with a hard proximal cap making lesion engagement and penetration difficult. It can also result in sub-stent wire tracking, particularly with stiff, penetrative wires, which prevents subsequent passage of balloons and stents even if distal true lumen is reached. As reported in several studies, IS CTOs are longer [1, 2], tissue is often harder, not due to calcifications but to fibrous and compact neo-intimal proliferation. An ostial location has also been found to predict procedural failure [2]. Moreover, presence of prior stents interfere with microcatheters, balloons and new stents. Obviously, stent-fractures, undersized stents, deformed and malapposed stents might increase the difficulty to cross with wires, balloons and stents.

The hybrid strategy has been shown to be effective for increasing success rates with IS CTOs, with technical and procedural success now similar in patients with CTOs due to ISR and de novo CTOs, (technical success 89.4 % vs. 92.5 %, $P = 0.43$; procedural success 86.0 % vs. 90.3 %, $P = 0.31$). In their multicenter study, Christopoulos et al. showed that the most common crossing approach was antegrade wire escalation (41.1 %), followed by the retrograde approach (31.4 %), and antegrade dissection and re-entry (27.4 %). The CrossBoss catheter was used in 54.4 % of cases (26.7 % of de novo CTO cases) [1].

Antegrade wire escalation has been historically used as a first approach, and is still the preferred technique for crossing in-stent CTOs for most operators, although the CrossBoss is now a very helpful tool to add for improved success (Fig. 10.2). Inability to cross the occlusion with a guidewire is the main mode of technical failure, whereas inability to advance or fully inflate a balloon catheter accounts for a minority of cases. As for de novo CTOs, there is no general rule of treatment, as lesion characteristics are highly variable and hardly predictable before a proper dual injection is performed. Soft tip tapered polymer-jacketed wires (such as the Fielder XT) can be first tried a few minutes to search for any central in-stent micro channel, but our experience with this wire in IS CTOs has been deceiving. These soft wires are less steerable and may also slip outside the stent structure, in the sub-intimal plane. Therefore, escalation goes quickly to stiffer polymer jacketed such the Pilot 200 with a special attention not to track the wire under the stent struts. But the most useful guidewire family in that situation are the high torque and hard tip wires like the Miracle 12 which provide a very acute control and torque of the tip to allow the wire to stay within the stent. Because the wire is non-tapered, it is less likely to exit through a stent strut. Several orthogonal views should be taken in order to visualize the wire track within the stent (Fig. 10.2). Hard and tapered wires can be interesting to puncture the proximal cap or go for a short distance trough very hard tissue. In our experience, the Confianza Pro 12 has very good torque control and should be

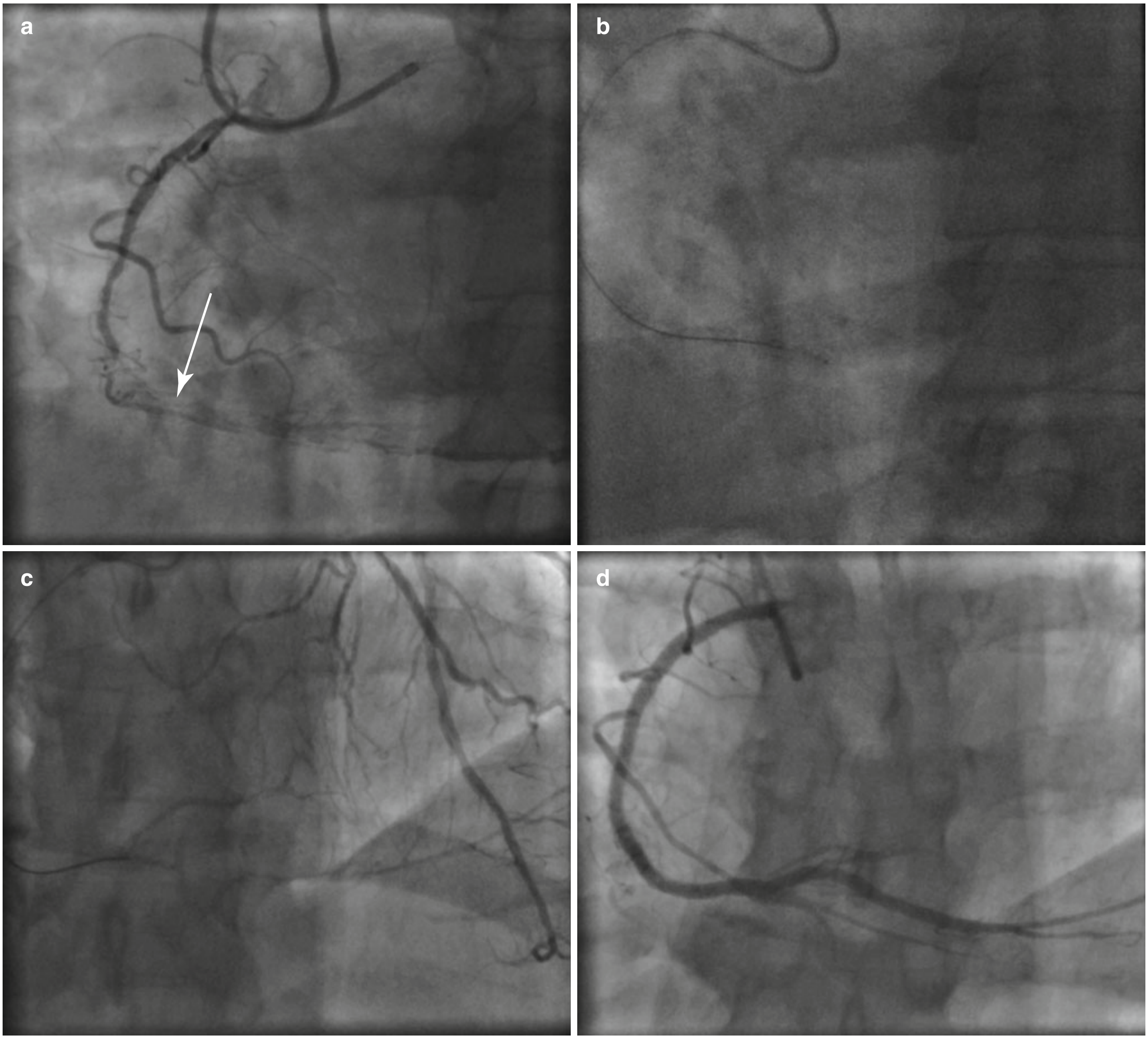

Fig. 10.2 In-stent restenotic CTO. (**a**) Long in-stent occlusion in the distal RCA ostium, likely due to an in-stent restenosis as highlighted by the presence of an island of patency with contrast at the beginning of the occlusion. (**b**) CrossBoss navigates into the stents and (**c**) is advanced true-to-true into the PDA. (**d**) Final result after deployment of DES

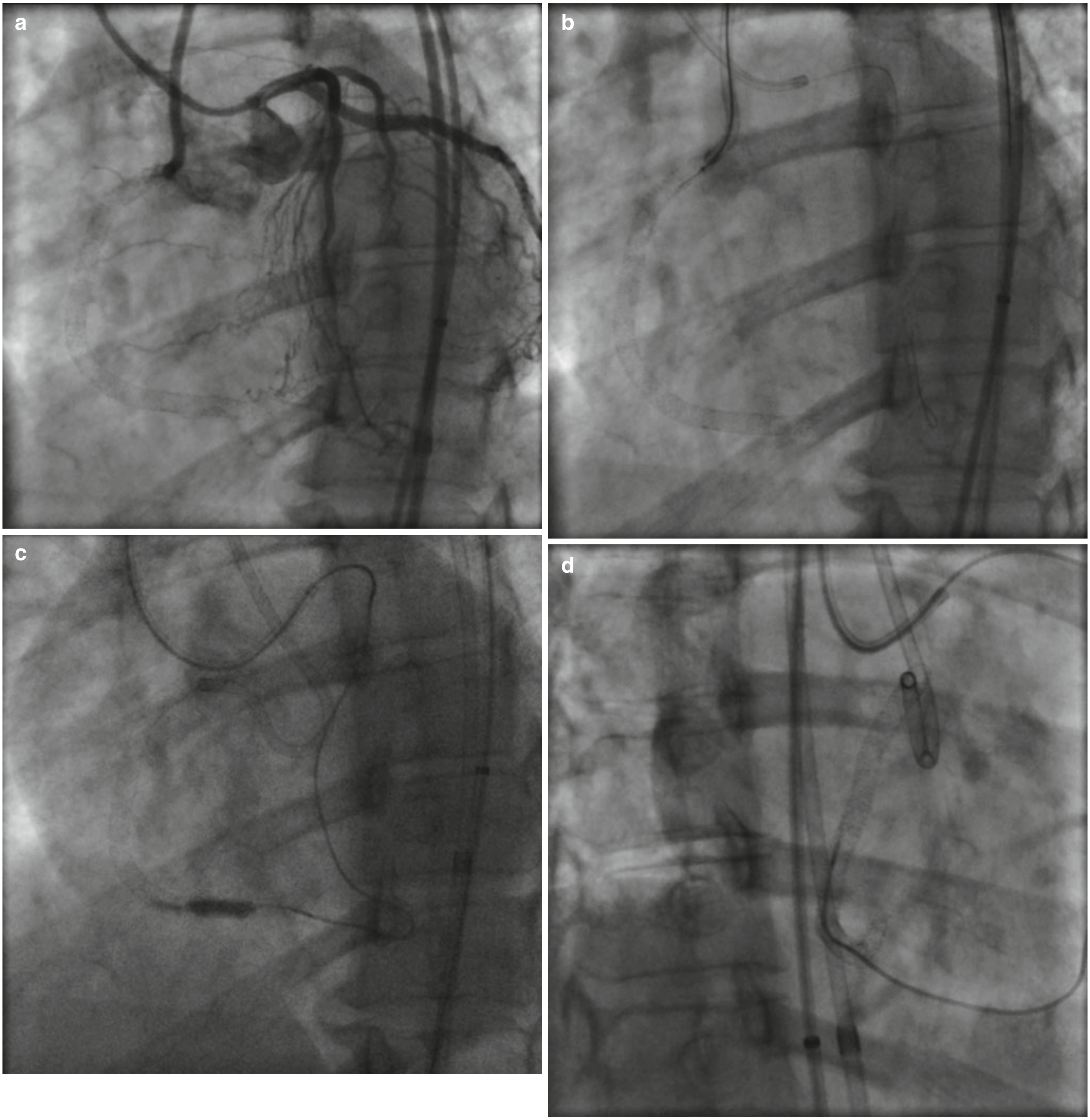

Fig. 10.3 In-stent CTO from a previous stent thrombosis. (**a**) Very long in-stent occlusion from the RCA ostium to the crux, due to a documented stent thrombosis few years ago. (**b**) This is impossible to progress with the CrossBoss into the occluded stents. (**c**) Antegrade guide changed for an AL0.75. No success with CrossBoss. Retrograde approach and distal contrast injections to modify the plaque. (**d**, **e**) Careful navigation with an alternative use of Pilot 200 and Confianza Pro 12 guidewires to stay within the stents. (**f**) Final result after deployment of DES

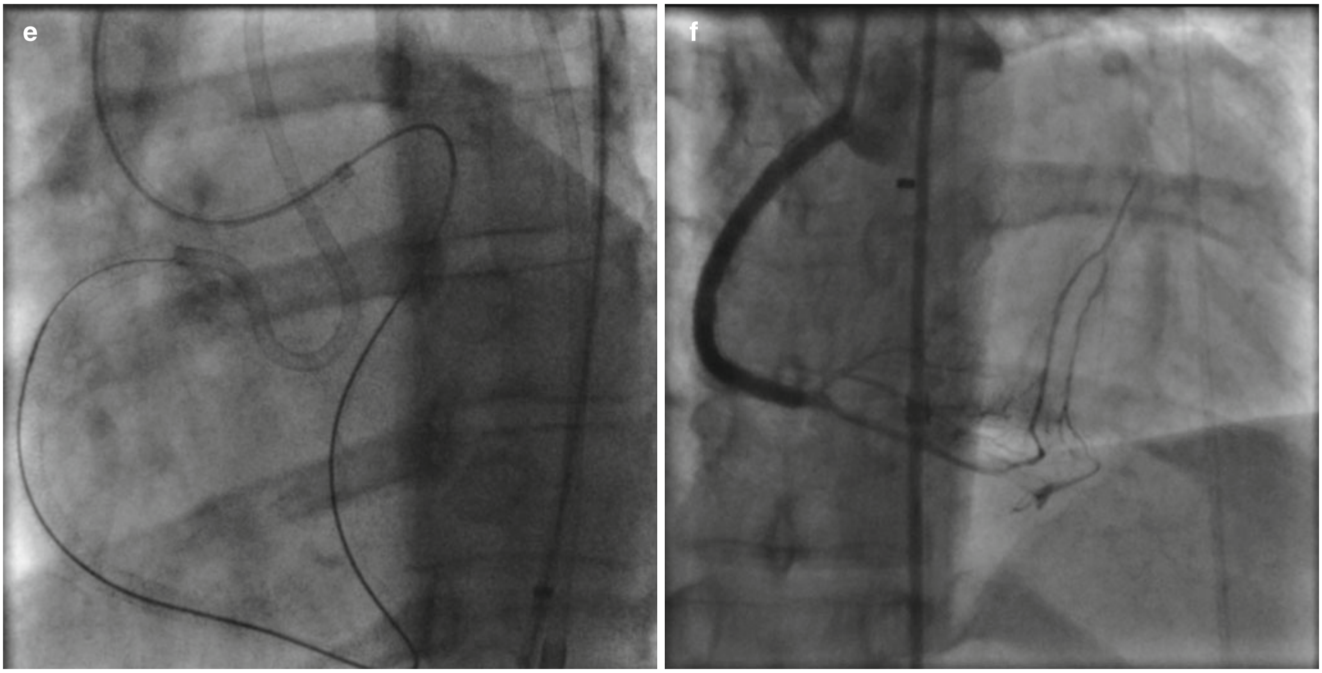

Fig. 10.3 (continued)

preferred to polymer-jacketed stiff tapered tip like Progress 200 T which can easily slip under the struts. Nevertheless, the latter wire, due to its slippery characteristics, is interesting during cases of very fibrotic and hard restenotic tissue and could facilitate wire progression. Finally, the Gaia family wires have emerged as very efficient wires for in-stent occlusions. Given that the ambiguity of the vessel course is limited with IS CTO, the Gaia wires, especially the less tapered Gaia 3rd version, can be very effective; the wire is pushed up to deflection of its tip. Then, the wire is pulled and redirected away from the resistance. Several orthogonal views should be taken to confirm that the wire stays within the border of the occluded stents.

Although very useful in CTO PCI, knuckled wires should be avoided as a first strategy because of the absence of cleavage space within an IS CTO. Such knuckled wires can track under the stent struts or in the subintimal sub-stent space, resulting in crossing outside the stent structure. Although it has been described [7] with successful stenting in the subadventitial layer under the previous occluded stent, extreme caution should be applied for the following reasons: (1) although sub-intimal stenting appears to be safe in the majority of cases, stenting outside a previously deployed stent can lead to substantial overstretching of the adventitia, as a result of non-compressible in-stent tissue leading to potential perforation. (2) Distal re-entry can be laborious and (3) outcomes are unknown with this technique. The key point of a wire-based strategy is to enter the proximal cap in the "true lumen" and avoid to track underneath the stent struts. If the cap is blunt and hard, inflating an OTW balloon (adapted to the size of the proximal vessel) a few millimeter upstream to the in-stent CTO segment can help, as with the performance of an anchoring balloon technique. The back-up support for wire puncture is therefore stronger. Moreover, this technique allows a very good coaxial alignment of the wire in order to puncture the center of the proximal cap instead of the sub-stent space. The Venture catheter is a steerable and orientable micro-catheter that sometimes can be used successfully used with or without Stingray guidewire in that kind of situation [8]. Again, orthogonal angiographic views should be taken most of the time without contrast injection in order to confirm that the wire tracks within the stent borders. If the wire crosses into the distal true lumen but no microcatheter or balloon can cross the occlusion, several solutions could be sought. The first is the CrossBoss catheter that could cross as described later, even over the wire [9]. But in cases of very fibrous and hard tissues we recommend the use of the Tornus or the Corsair microcatheters that can be screwed into the lesion using counter-clockwise motion [10]. After crossing with the microcatheter, the crossing wire can be exchanged for a high support soft tip wire to complete the procedure. However, if the wire crossed outside the stent structure and re-entered more distally, it is wise not to pursue with Tornus or Corsair, as both can get entrapped within the stents struts. In such cases, sequential balloon dilation starting with a very small balloon is the preferred approach, leading to strut enlargement and ability to deliver subsequent new stents in the segment.

The utility of the CrossBoss catheter for refractory CTOs has been established in the FAST-CTO trial [11]; however, ISR cases were excluded from this trial. First description was done in a multicentre European study reporting CrossBoss and Stingray devices for refractory CTOs [12]. The only case of ISR CTO within this study was successfully completed with CrossBoss catheter alone.

Other small series now support the use of CrossBoss catheter for IS CTOs. Indeed, the success rate of crossing with the CrossBoss alone is between 83 % as reported by Papayannis et al. [9] (5 of 6 patients) and 90 % (28 of 31) as reported by Wilson et al. [4]. In that latter study, use of the CrossBoss catheter was the primary strategy in 60 % of IS CTOs cases (31 of 52). Christopoulos et al. reported a use of the CrossBoss for IS CTOs of 54.4 % with a final technical success of 89.4 % [1]. Direct lumen-to-lumen crossing of the catheter was achieved in 88 % of cases in the Wilson et al. series [4], avoiding thus the need for re-entry as long as the distal cap of the CTO is either within or at the very end of the stent struts. Of course, larger series are needed to collect more data.

Efficacy of CrossBoss catheter is based on the fact that stent struts tend to prevent device exit into the subintimal space and ease the passage of the catheter's blunt tip to the distal true lumen. Use of the CrossBoss can lead to a reduction in procedural time. Indeed, the UK ISR-CTO registry reported a median crossing time of the occluded stents of 8 min [4]. Wilson et al. didn't find any differences in baseline characteristics between successful or failed CrossBoss cases. Nevertheless, a few mechanism of failure with the CrossBoss have been reported [4, 9] such as underdeployed stent struts especially with small size stents, tortuosity (defined as a bend more than 45°) within the stented segment which can lead to the CrossBoss tip catching on the stent struts. Although tortuosity proximal to the occlusion does not appear predictive of failure, an occlusion that sits proximal to the stent may be difficult to engage with the device, and may therefore require stiff wires to puncture within the stented segment. Ostial location is a frequent cause of failure probably because of the need for tremendous backup to engage the proximal cap with the CrossBoss catheter. The retrograde approach should be considered if possible in this situation. CTO length and vessel diameter don't seem to predict CrossBoss failure [4]. In the early experience of CB for ISR CTOs [12] and some other series [9], presence of a side branch at proximal cap has been reported as a predictor of failure, but was not found in the UK experience series [4] nor in five high-volume CTO PCI US centers [1]. Although this is poorly documented, it is our belief that stents that occluded as a result of a prior thrombosis offer more resistance to wire and CrossBoss compared to stents that present islands of patency (Fig. 10.3).

In the case of antegrade wire-based or CrossBoss-based failure, a retrograde approach should be considered especially in case of ostial IS CTO [7, 13] (Fig. 10.3). As for de novo CTOs, distal cap is less exposed to systemic blood pressure and tends to be softer allowing wires to penetrate and progress. Of course, antegrade and retrograde techniques should be combined to complete the case. The general principles of the retrograde approach apply here as well, with the exception of the crossing strategy. Although long de novo CTOs will be crossed with retrograde dissection re-entry using knuckled wires, such a technique should be also avoided from the retrograde side, as they will also track underneath the stent. Efforts to stay within the stented segment should be made. The use of the retrograde, in addition to the antegrade approach, can facilitate progression of wires from either sides, serving as targets to one another. The same kind of wires described above for the antegrade escalation strategy should be use to keep maximum steerability and control while traveling retrograde within the stent.

Problem-Solving Strategies

Sub-stent Wiring

Especially when hitting stent fractures or malapposed struts, the wire could be at some part tracking under the struts or leaning against struts and thus blocking passage of devices. In these particular situations, Rotablator can be used [14]. After exchanging the 0.014′ wire for a RotaWire, cautious advancement of a small burr (1.25 mm most of the time) can be done. Very slow motion and also slow rotational speed should be used in order to avoid burr stalling and trap beyond the struts or the fibrous lesion. This technique will lead to an ablation of the malapposed struts and will allow advancement of balloons and stents.

In the same way, excimer coronary laser atherectomy can be used. The advantage is that the 0.014′ wire used to cross the in-stent CTO is ready to support the laser device and doesn't need to be exchanged [15]. Moreover, the laser has the ability to ablate tissue that extend beyond the stent borders, increasing the chances of better subsequent apposition. However, laser will not ablate metal struts.

Sub-stent Subintimal Strategy

If the CrossBoss fails to connect to the true lumen, if antegrade or retrograde wiring fail, subintimal tracking can be used in selected cases. As described by Lee et al. [16], this maneuver is challenging but safe and leads to good midterm outcome, especially if performed in patients who underwent prior cardiac surgery. Re-entry should be performed at distance to the occluded stent using tapered stiff guidewires, the Stingray balloon or from the retrograde side with the reverse-CART technique. In such situation, a new subintimal lumen is created and the occluded stent and its proliferative tissue crushed by balloons and new stents, as mentioned earlier. Sub-stent passage of devices is usually possible as for other subintimal strategy techniques. Nevertheless, crushing occluded stents is difficult and needs cautious sequential dilatation followed with placement of a new stent with high radial strength. Extreme care should be applied not to overstretch the vessel with the new stents; it is safer to accept some under sizing of the newly implanted stents to avoid vessel perforation due to adventitial over dilation.

Conclusions

IS CTOs are identified entities that carry their own predictors of success and mechanisms of failure that differ from de novo CTOs. PCI of IS CTO has traditionally been associated with lower success mainly due to wire crossing difficulties. The hybrid strategy, especially including the CrossBoss catheter, seems to be associated with similarly high procedural success and low major complication rates as for patients with de novo CTOs.

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