EuroIntervention 2021;17:e611-e612 published online e-edition October 2021

In-stent CTOs: same story with a different conclusion?

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Chronic total occlusion (CTO) is a common finding, identified in around 20% of patients with coronary artery disease (CAD)[1]. There has been a recent global growth of procedures, with increasing rates of success, aided by advances in technology and successful application of systematic approaches such as the hybrid algorithm. As the number of patients undergoing revascularisation for non-occlusive CAD continues to rise, occlusive in-stent restenosis (ISR-CTO) is also likely to increase. Although bare metal stents (BMS) have been completely superseded by drug-eluting stents (DES), which are less prone to ISR, in the last decade, ISR-CTO still comprises a significant proportion of all CTOs, with estimates of prevalence approaching 15%[2]. Optimal management strategies to ensure the best patient outcomes have yet to be determined, as scoring strategies developed to define lesion-level complexity have largely failed to include ISR-CTOs.

The challenges of ISR-CTO relate in part to the histologically different patterns of occlusion that occur within stent when compared with *de novo* lesions. Anatomical and intravascular ultrasound (IVUS) data have demonstrated that neointimal hyperplasia is the most frequently identified pathology, often co-existent with organised thrombus with the occlusive tissue comprised of proliferating vascular smooth muscle cells surrounded by a tough collagenous matrix[3]. Typically, there are no discernible microchannels to allow the passage of soft, tapered wires, and escalating attempts with higher tip-load or polymer-coated wires increase the risk of extra-stent, subintimal penetration[4]. Whilst the presence of the radiopaque stent acts as an architectural guide, thereby removing anatomic ambiguity, wiring through struts and subsequent difficulties in equipment delivery can hamper progress and result in either conversion to a retrograde approach or technical failure.

Despite these inherent complicating factors and early difficulties, recent data demonstrate surprisingly good procedural results, similar to *de novo* CTO. Reports from large registries in Europe, North America and Asia have all indicated procedural success rates of 85-90%, with low complication rates and in-hospital major adverse cardiac events (MACE)[5-8]. However, as promising as this seems, it is critical to note that lesion complexity was low in some of these studies, with retrograde approaches not well represented. Lesion morphology between ISR-CTOs varies considerably, and procedural success and the risk of in-hospital complications still largely depend on anatomical characteristics such as lesion length, tortuosity, and calcification.

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DOI: 10.4244/EIJV17I8A109

This important point is addressed by Sekiguchi et al in this issue of EuroIntervention, wherein they define four key occlusion patterns of ISR-CTO (A to D), to compare the broad PCI strategies employed, and immediate technical and procedural success rates in a large sample (N=791) of patients with ISR-CTO taken from the Japanese CTO Expert Registry 2015-2018[2].

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In brief, pattern A refers to ISR-CTO completely within stent; pattern B is ISR-CTO extending >5 mm beyond the distal stent edge; pattern C is ISR-CTO starting >5 mm before the proximal stent edge; and pattern D is ISR-CTO starting before and extending beyond the proximal and distal stent edges >5 mm, respectively (Central illustration)[2].

Pattern A was the most frequent, comprising 53% of cases and, predictably, technical success was highest in this group at 96.2% compared with 86.2%, 92.9% and 75.4% in patterns B, C and D, respectively ($p<0.001$). There was nearly 98% guidewire success in pattern A, with lower use of contrast, fluoroscopy, and procedural time. Complications overall were remarkably rare, with one patient death and low MACE rates for the given population. The procedural strategy employed in each pattern also varied significantly with 90.9% antegrade alone for pattern A, whilst a primary or rescue bidirectional approach was needed in two thirds of cases in pattern D, although precise procedural data regarding technique are not given.

How does this study inform us?

Pattern D represents the most challenging type of lesion, and in fact the authors report that lesion length, tortuosity, and J-CTO score were all significantly higher at baseline. The obvious immediate conclusion to draw from this is that careful preprocedural assessment of the patient and the angiographic data remains key, and that more difficult cases should only be attempted with relevant expertise on hand. These data would suggest that less experienced CTO operators should be confident to attempt within-stent CTO-ISRs (subset A), although even in the "easier" pattern A cases there was a 5% chance of conversion to retrograde. Fundamental elements of good CTO practice such as dual catheter injections should still be used. More complex, pattern D cases should be performed by expert operators comfortable with the retrograde approach where the procedure is likely to be longer, more complex, and less likely to be successful.

Whilst these findings of this study are consistent in terms of immediate procedural success, they add little to the more important issue of longer-term patient outcome. When follow-up data are available, there have been mixed messages, and the benefit of ISR-CTO PCI has not been confirmed on a patient level[5,8,9]. Whilst angina and MACE are reduced in successful ISR-CTO PCI compared with failed procedures[8], it is not yet understood how this treatment compares with other options such as surgical coronary artery bypass grafting (CABG) and optimal medical therapy. Although favourable outcomes have been observed in *de novo* CTO PCI when compared with CABG[10], the disease process is demonstrably different in ISR-CTO, and these results are not necessarily extrapolatable. Even when immediate recanalisation is achieved, complicating factors including the presence of at least one pre-existing layer of stent, and the presence of existing demonstrable stent failure may reduce the chances of long-term freedom from symptoms and cardiac events. Registry data in a non-CTO ISR population would suggest that long-term outcomes may be significantly worse than in *de novo* PCI, with higher rates of target vessel failure and MACE over several years of follow-up[11].

Finally, for research to be of value, it must speak to both patients and physicians. Whilst this study adds to confidence that ISR-CTO is safe and frequently successful, it is quality of life and durable freedom from cardiac events that matter to patients. This shared objective should be at the forefront of physicians' minds when developing the evidence base in this critically important area.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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