AsiaIntervention
2025;11:e97-e98
published online e-edition July 2025
DOI: 10.4244/AIJ-E-25-00004

EDITORIAL

Ultrathin-strut stents – towards zero stent-related events?

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While the development of metallic stents revolutionised percutaneous coronary intervention (PCI) and solved the problems of acute recoil and vessel closure, thus making the acute results safer, it brought about a new stent-related issue of restenosis related to inflammation caused by the metal struts. The search for a solution to this problem led to the first-generation drug-eluting stents (DES), which reduced restenosis but created a new problem of impaired vascular healing, leading to late and very late stent-related events. Furthermore, progress in biomaterials, from stainless steel to cobalt/platinum chromium, allowed for thinner struts while maintaining radial strength and radiopacity. In parallel, the development of biocompatible polymers and advanced polymer-coating technology led to further development of newer stent technology – the second-generation DES – with faster healing of endothelium. For over a decade, other developments, including bioabsorbable polymers and polymer-free DES, while showing non-inferiority, failed to deliver on the promise of late superiority (after bioabsorption of the polymer)[1]. Technological advancements, including laser-cut stents, led to the development of ultrathin-strut DES (<70 µm)[2], and meta-analyses have shown clinical superiority of ultrathin-strut DES over thin-strut DES[2]. These platforms have strut thicknesses between 50 µm and 65 µm: changes in stent design retain adequate radial strength despite the ultrathin strut; they have a bioresorbable polymer and elute sirolimus. Whether the strut thinness, the bioresorbable polymer, the drug, or their combination is responsible for the superiority has been debated[3].

In this issue of AsiaIntervention, Protopopov et al present the results of the S-FLEX Russia registry evaluating the ultrathin-strut Supraflex Cruz sirolimus-eluting stent (Sahajanand Medical Technologies Ltd.) in a real-world all-comers Russian cohort of 522 patients undergoing PCI. In a cohort with 24% of patients with diabetes, 38% with multivessel disease, 21% with moderate to severe calcification, and only 36% undergoing post-dilatation, and with data on intravascular imaging not reported (and likely very low), stent failure events were extremely low. There was 1 patient (0.2%) with stent thrombosis and 5 patients (1%) with target lesion revascularisation, with a target lesion failure (TLF) rate of 3.1% at 1 year, consistent with other registry data from the same stent platform[4].

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While it is tempting to indirectly compare these rates to other platforms, this is fraught with limitations due to differences in the enrolled cohort, event definition, reporting, and adjudication. Nevertheless, the results continue to be encouraging despite the less-than-optimal PCI performed to current standards, including the very low use of intravascular imaging. While the ultrathin-strut platform and stent design can by itself significantly improve clinical outcomes, the higher rate of events in complex coronary disease, including bifurcation, is still an attestation of the need to optimise PCI using intravascular imaging[5].

Will we ever have zero stent-related events? Stent-related events can be broadly categorised into events directly related to the stent or those indirectly related to the stents or due to patient characteristics. The ones directly related to the stent include endothelial damage; inflammation due to a foreign body reaction around struts/polymer, resulting in delayed re-endothelialisation, neoatherosclerosis, and longer-term increase in smooth muscle cell proliferation resulting in

restenosis; flow disturbances around the struts increasing the risk of stent thrombosis; and metal ion leak over the long run resulting in chronic inflammation. The thinner struts and better polymers address many of these issues with lower inflammation, faster re-endothelialisation, and laminar flow around the struts reducing the risk of stent thrombosis/restenosis. However, it is not clear if making the struts even thinner would provide any incremental benefit. Intravascular imaging-guided post-PCI optimisation has been shown to improve clinical outcomes[6]. Whether this benefit is also seen in patients undergoing implantation of ultrathin-strut stents is not known. However, stent malapposition or underexpansion can increase the effective strut thickness and thereby negate any beneficial effect of ultrathin-strut stents, and as such, intravascular imaging-guided optimisation should theoretically help. A dual-therapy CD34 antibody-covered SES (dual-therapy stent [OrbusNeich]), which is an SES with CD34 antibodies immobilised on its luminal surface to capture circulating endothelial progenitor cells and promote early endothelialisation, has been tested to reduce stent-related events, including neoatherosclerosis. However, the rate of target lesion revascularisation was higher when compared with second-generation DES[7], likely due to thicker struts (100 microns) and the potential differentiation of endothelial progenitor cells into smooth muscle cells.

One other potential disadvantage of the current metallic DES platform is the "caging" of the artery due to the metallic scaffolding inhibiting natural pulsatility, vasomotion, and adaptive remodelling, the relative contribution of which to stent failure is not clear. To address this, bioabsorbable scaffolds were developed to uncage the artery after bioabsorption but, so far, have failed to prove superiority over metallic DES. The DynamX coronary bioadaptor system (Elixir Medical) is a novel platform that can unlock and provide dynamic support to the artery, allowing it to regain its natural pulsatility and vasomotion. In the INFINITY-SWEDEHEART trial comparing the DynamX bioadaptor versus the zotarolimus-eluting DES (Resolute Onyx and Onyx Trustar [Medtronic]), the DynamX bioadaptor was non-inferior to contemporary DES for TLF at 1 year. Interestingly, in a prespecified landmark analysis after 6 months (when uncaging happens), the rate of TLF was lower with the DynamX bioadaptor compared with contemporary DES[8]. Longer-term follow-up is awaited. Finally, stent failure or vessel failure are also related to a host of patient-related factors including comorbidities (advanced age, diabetes and chronic kidney disease).

The near future incremental advances in PCI with the potential to reduce clinical events will likely come from appropriate lesion selection, optimal stent implantation using a combination of physiology and intravascular imaging with artificial intelligence application, and advances in medical therapy, and will less likely be due to any incremental changes in stent design. Up until that point, the incremental clinical benefit observed with ultrathin-strut platforms, including that of the Supraflex Cruz, should challenge prior completed trials, including the inferior results seen with PCI (using the TAXUS [Boston Scientific] or CYPHER [Cordis Corporation] stents) compared with coronary artery bypass surgery (CABG) in patients with diabetes in the FREEDOM trial. In fact, the TUXEDO-2 trial, enrolling a FREEDOM-like cohort, has just completed enrolment and will provide further insights into the outcomes with modern DES versus the performance goal of CABG from FREEDOM[9]. While aiming for zero stent-related events is likely unrealistic, we are slowly but surely chipping away at stent-related events, making PCI safer and longer-lasting despite an ever-increasing patient complexity. In the meanwhile, let us not forget the basics of appropriate patient/lesion selection, optimising PCI outcomes with intravascular imaging, maximising medical therapy, and encouraging a healthy lifestyle.

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Conflict of interest statement

S. Bangalore reports grants and personal fees from Abbott; and personal fees from Boston Scientific, Biotronik, Pfizer, Amgen, Inari Medical, Truvic, Recor Medical, and Reata outside of the submitted work.

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