Treatment of patients with diffuse coronary disease: a challenge yet to be solved?

Tim Kinnaird1,2, Mamas A. Mamas2,3

1 Department of Cardiology, University Hospital of Wales, Cardiff, United Kingdom
2 Keele Cardiovascular Research Group, University of Keele, Stoke-on-Trent, United Kingdom
3 Department of Cardiology, Royal Stoke Hospital, University Hospitals of North Midlands, Stoke-on-Trent, United Kingdom

In the early days of coronary intervention, cardiologists performing percutaneous coronary intervention (PCI) were keenly aware that there was a cost in terms of repeat target lesion revascularization (TLR) with the use of longer lengths of bare metal stents (BMSs). A study combining data from 6 BMS trials illustrated this, with each 10 mm of additional stent length associated with an absolute increase in percent diameter stenosis of 7.7% at 6 to 9 months of angiographic follow-up (P < 0.0001).1 In a subsequent comparison of BMSs to first generation drug-eluting stents (DESs), the absolute increase in percent diameter stenosis per 10 mm at angiographic follow-up of sirolimus-eluting DES (3.5%) was significantly lower than that observed with BMS (9.1%, P < 0.0001).2 Therefore, although there was still a price to pay associated with the use of long lengths of first-generation DES stents, it was lower in comparison with BMS. In contemporary PCI practice with increasingly deliverable platforms and an ethos of normal-to-normal vessel stenting, the use of long lengths of DES is a common practice. Indeed, several stent manufacturers now market stents of 48 mm in length.

In the current issue of the Polish Archive of Internal Medicine (Pol Arch Intern Med), Paszek et al3 investigated the device and patient outcomes of PCI procedures involving long stent lengths of second generation everolimus- or zotarolimus-eluting stents (defined as a total stent length of more than 30 mm). In this single-center study of 290 patients, procedure-related adverse outcomes were relatively frequent. At a median follow-up of 831 days, the overall repeat revascularization rate was 15.8%. Of this, however, TLR for restenosis accounted for only 3.1% of repeat procedures, with the majority being performed in de novo lesions. Furthermore, stent thrombosis (ST) occurred relatively frequently with a definite/probable ST rate of 7.2%. The long period of follow-up also allowed the investigators to identify that a significant proportion of the thrombotic events occurred after completion of the standard period of dual antiplatelet therapy (DAPT). Interestingly, there were no procedural factors that predicted an increase in repeat revascularization, although several patient factors, including chronic kidney disease and peripheral vascular disease, were associated with adverse outcomes.

Although the study has several strengths, including the real-world setting and long follow-up, its limitations include relatively modest numbers accumulated over an extensive period, data obtained from a single center, and an arbitrary definition of long stent length. Nevertheless, the study findings have several implications for clinical practice and raise questions about the optimal management of patients with long lengths of coronary artery disease. Although the low rate of TLR for restenosis implies that the second-generation DES platforms are effective in suppressing neointimal proliferation and perform well in the real-world practice, the frequent repeat revascularization for non-TLR lesions is an important finding. One might postulate that this is a result of the diffuse nature of the atherosclerosis underpinning the need for long stents at the index procedure. These data are clearly important when deciding on the preferred revascularization strategy in a patient with diffuse disease, and in weighing up the relative merits of surgical revascularization versus PCI necessitating the use of long lengths of stent. It is also of some concern that 1 in 14 patients experienced a definite or probable ST, an event which often has catastrophic consequences for the patient. This observation coupled with the frequent occurrence of ST late after completion of the recommended DAPT course, highlights the importance of not only optimizing stent apposition and expansion at the index procedure, but also tailoring choice and duration of DAPT therapy afterwards.
Can the outcomes of patients treated with long lengths of stents be improved? The use of fractional flow reserve or other resting indices such as instantaneous wave-free ratio are not reported in the current study but their use might optimize the index procedure not only in identifying culprit lesions within long lengths of disease and thus potentially reducing the total length of stent but also physiologically assessing remote disease to allow treatment and reduce the frequency of repeat interventions at a later date. Furthermore, in the current study, the use of intravascular ultrasound imaging was low with only 14.1% of procedures utilizing this technology. There is growing evidence from observational studies and randomized controlled trials that intravascular imaging guidance not only enhances the acute procedural result following PCI, but also improves longer-term clinical outcomes. For example, in a meta-analysis of 31 studies with 17,882 patients, intravascular ultrasound imaging-guided PCI was associated with lower rates of all-cause mortality (OR, 0.74, 95% CI; 0.58–0.98), myocardial infarction (OR, 0.72; 95% CI, 0.52–0.93), TLIR (OR, 0.74; 95% CI, 0.58–0.90), and ST (OR, 0.42; 95% CI, 0.20–0.72) compared with angiographically-guided PCI. Therefore, more routine use of intravascular imaging in cases involving long lengths of stents should be encouraged, as advocated by the recent expert consensus document on the use of intracoronary imaging by the European Association of Percutaneous Cardiovascular Interventions.

It might also be possible to further ameliorate the excess of ST associated with the use of long lengths of stent by using more potent antiplatelet regimes. In the current study, the use of a more potent P2Y12 inhibition was low. However, both prasugrel and ticagrelor have separately been proven to reduce the incidence of ST as compared with clopidogrel. Prolongation of DAPT duration might also mitigate the late ST observed in the current study. In the Dual Antiplatelet Therapy After Drug-Eluting Stents trial, an additional 18 months of clopidogrel therapy significantly reduced the rate of ST compared with the standard 12-month duration (0.4% vs 1.4%, respectively; \( P < 0.001 \)). The findings of the current study support the concept of more frequent use of potent P2Y12 inhibitors and/or prolonging DAPT therapy duration when long lengths of stent are used, and in particular when patients have evidence of vascular disease elsewhere. However, considerations to use more potent P2Y12 inhibition or to prolong its duration must also balance the excess bleeding risk associated with its use against any potential ischemia reduction.

Whilst previous studies have suggested that the advent of newer generation DES (and newer, more potent antiplatelet therapies) has favorably modified the relationship between increasing stent length and major adverse cardiovascular events, the current study highlights that there are still challenges to be met in the management of patients with diffuse coronary disease.

**REFERENCES**


