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EDITORIAL COMMENT

The Long Road to Optimal Stenting of Diffuse Coronary Artery Lesions*

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Advances in stent design and technology over the past few decades have markedly decreased the current rates of in-stent restenosis (ISR) compared with those of bare metal stents and earlier first-generation drug-eluting stents (DES).[1,2] Nonetheless, ISR remains the Achilles' heel of stents today, and longer stent length in the presence of diffuse coronary lesions is an independent risk factor for ISR and stent thrombosis even in the contemporary era of second-generation DES.[2-6] The question of what primarily drives restenosis-stent diameter or length-is particularly challenging to determine in diffuse lesions because the vessel typically tapers substantially. Hara et al[7] published an analysis of the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial looking specifically at the impact of total stent length and average nominal stent diameter on 10-year mortality after percutaneous coronary intervention (PCI). Interestingly, they found that total stent length and small stent diameter (<3 mm) were significantly associated with long-term mortality, although average stent diameter measured as a continuous variable failed to demonstrate an association.

The treatment of diffuse lesions is quite relevant because they comprise roughly 20% of PCI today, a proportion that we suspect will only continue to increase given the increasing incidence of diabetes mellitus and surgical turndowns in very elderly patients.[8] However, data on the comparative effectiveness and safety of various current second-generation stents in the setting of diffuse coronary lesions are limited, and hence the question of which stent platform has the best performance for diffuse coronary lesions remains largely unanswered.

It is with this backdrop that we read with keen interest the study by Kang et al[9] in this issue of *JACC: Asia,* in which the authors provide a comprehensive synthesis of the available randomized clinical trial data on this relevant subject. Specifically, the investigators conducted a pooled analysis of patient-level data of 1,450 South Korean patients with de novo diffuse (≥25 mm) coronary lesions from 3 randomized clinical trials[10-12] comparing the outcomes of 5 different types of DES: cobalt-chromium everolimus-eluting stents, platinum-chromium everolimus-eluting stents, resolute zotarolimus-eluting stents, biodegradable polymer biolimus-eluting stents, and first-generation sirolimus-eluting stents. The primary endpoint was angiographic in-segment late lumen loss at 9 months. Key secondary endpoints included all-cause death, myocardial infarction, target-vessel revascularization (TVR), stent thrombosis, and major adverse cardiovascular events (composite of all-cause death, myocardial infarction, and TVR) at 1 year. Differences in baseline patient characteristics were adjusted for using inverse probability of treatment weighting. The investigators found no appreciable difference in in-segment late luminal loss at 9 months between the various DES platforms (P = 0.38). The range of in-segment luminal loss spanned from 0.10 ± 0.37 mm in the sirolimus-eluting stents group to 0.17 ± 0.41 mm in the cobalt-chromium everolimus-eluting stents group. Regarding clinical outcomes, there were no significant between-group differences in all-cause death, myocardial infarction, TVR, stent thrombosis, or major adverse cardiovascular events at 1 year.

The authors should be congratulated for this excellent work. To date, this pooled patient-level

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analysis represents the largest study to examine the efficacy of current generation DES in the setting of diffuse lesions. Additional strengths of the study include: 1) generalizability because of the inclusion of several patient/biological phenotypes (ie, stable ischemic heart disease and acute coronary syndrome) and DES platforms; 2) blinded core laboratory imaging analysis using quantitative coronary angiography; and 3) comprehensive 1-year clinical outcome data, although the analyses were underpowered to detect meaningful differences in these endpoints.

However, there are some limitations worth considering when interpreting these data. First, angiographic endpoints for ISR are less sensitive than intracoronary imaging-guided ones, such as minimal stent area, which has consistently been shown to predict long-term PCI outcomes, including in patients with diffuse lesions.[13,14] Second, only 71% of the enrolled patients underwent follow-up angiography, raising the possibility of selection bias. Third, the study had relatively short-term follow-up—only 9 months for angiographic outcomes and 12 months for clinical outcomes. This is relevant because prior studies have reported a linear and sustained accumulation of stent-related events (roughly 2% per year) between 1 and 5 years after PCI across several DES platforms.[15] Last, regional practice patterns, such as the relatively higher use of direct stenting (10%) and intravascular ultrasound guidance (80%) in this South Korean cohort, must be considered when applying the data. Indeed, it is quite plausible that angiographic in-segment late lumen loss would be greater in an otherwise comparable US cohort caused by dramatically lower use rates of intravascular ultrasound.[16]

Despite these limitations, the data presented by Kang et al[9] are compelling. The investigators have demonstrated clinical equipoise of multiple different second-generation DES platforms for diffuse coronary lesions. This finding provides valuable reassurance to operators who may not have the full armamentarium of DES options at their disposal such that their decision of stent type will likely not impact the outcome of patients with diffuse coronary artery disease. Nevertheless, the management of diffuse lesions is constantly evolving; eg, there have been favorable outcomes with 48-mm-length everolimus-eluting stent platforms, which allow for less overlapping regions of stent in long coronary lesions.[17] Promising data such as these are needed to continue paving the long road to optimal stenting of diffuse lesions.

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