Coronary bifurcations lesions that involve significant side branches represent a particularly challenging subset of target lesions for percutaneous coronary interventions.\textsuperscript{1,2} Besides the necessity for the interventional cardiologist to often perform technically demanding interventions with more procedural steps,\textsuperscript{3} clinical outcome following percutaneous coronary intervention has usually been somewhat inferior. For more than two decades, coronary bifurcation lesions represent a serious touchstone for both interventional cardiologists and various types of stents and vascular scaffolds.\textsuperscript{1-6}

The use of first-generation drug-eluting stents (DES) has reduced the incidence of restenosis following percutaneous coronary intervention of bifurcation lesions as compared to bare metal stents. In a first, small-sized study by Colombo et al, a numerically lower rate of angiographic restenosis was seen in bifurcated lesions treated with a single DES in the main vessel.\textsuperscript{7}

In the meantime, pooled data of the Nordic Bifurcation and the British Bifurcation Coronary studies, both using first-generation Cypher DES (Cordis; Warren, New Jersey, United States), have clearly demonstrated at 9-month follow-up that clinical outcome is superior following a simple approach with provisional T-stenting of the side branch vs a complex approach.\textsuperscript{8} In addition, the Nordic Bifurcation study has shown that long-term outcome (up to 5 years) following bifurcation stenting with a simple approach was at least as good as the outcome of a complex approach.\textsuperscript{9} The aforementioned studies were performed with the first-generation Cypher stent that had a closed-cell design.

The results of several in vitro studies and bench tests suggest that DES with different stent materials and designs may act differently in the setting of bifurcation stenting.\textsuperscript{10,11} Moreover, the coatings of various DES types show significant dissimilarities in mechanical properties,\textsuperscript{12} which may be relevant during kissing balloon inflations that apply a significant shear stress to the coatings of DES. Consequently, the assessment of clinical outcome following bifurcation stenting with different types of DES is of great interest, in particular when performed in the setting of a randomized study.

In a remarkable original article published in Revista Española de Cardiología, Pan et al\textsuperscript{13} compare the 3-year outcome of 443 patients, in whom the simple approach for bifurcation treatment (provisional T-stenting of the side branch) was applied in a randomized manner, with either the first-generation, stainless steel, Cypher Select sirolimus-eluting stent (SES) (Cordis) or the second-generation, cobalt-chromium, Xience V everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, California, United States). The authors avoid use of the somewhat vague term “new generation DES”, which is currently embraced by many authors although it does not take into account the ongoing process of device evolution.

Pan et al. rather use the term “second-generation DES” when referring to Xience V, a choice that deserves broad approval as it places the device into the historical context of DES development.

Such information may help future researchers, as the cobalt-chromium EES is currently not the only EES available (eg, platinum-chromium based EES with either durable or biodegradable coating).\textsuperscript{14,15}

The study by Pan et al is characterized by the inclusion of many patients with acute coronary syndromes and diabetes mellitus, and by the excellent 3-year follow-up rate of 99.1\textsuperscript{13}

The considerable size of the present study was achieved by pooling data of 2 randomized DES studies, the SEAside study and the CORpal study.\textsuperscript{16,17} These studies were similar in various aspects, but there were also between-study differences. For instance, the visually assessed size of the side branch had to be $>$ 2.0 mm in SEAside and $>$ 2.25 mm in CORpal, and there were differences in the maximum side-branch lesion length and in the criteria for side-branch stenting.\textsuperscript{16,17} At 3-year follow-up, the composite end point of major adverse cardiac events, which in this study did not include periprocedural myocardial infarctions, was favorable for both DES types. An explorative subanalysis of late, major, adverse cardiac events (beyond 1 year) revealed a significant difference in favor of the EES.\textsuperscript{13}

Despite the randomization in both studies, the side-branch diameter was slightly larger in the EES group, which might have had an impact on outcome. Nevertheless, the present data from
Pan et al are very interesting, generate an attractive hypothesis, and show that studies exploring the long-term outcome of DES are warranted. In fact, the present manuscript by Pan et al should stimulate investigators to collect more high-quality data on coronary bifurcation treatment with a follow-up beyond 1 year.

In the SEASide and CORpal studies, bifurcations were treated by stenting the main vessel and – only if required according to predefined criteria – by (provisional) T-stenting of the side branch. As a consequence, the rates of side-branch stenting were low.\textsuperscript{16,17} While provisional T-stenting is currently considered the optimal approach for the vast majority of bifurcation lesions, this approach may not be optimal for the entire range of bifurcation lesions.\textsuperscript{7,9,18} In particular, in the presence of a heavily calcified side-branch ostium and/or a long side-branch length, operators may consider certain bifurcation lesions to be better suited for treatment with a 2-stent technique.\textsuperscript{1} Consequently, some bifurcation lesions with the abovementioned side-branch criteria may rightly not be considered for enrollment in studies that per protocol require use of the provisional T-stenting approach. In this light, the rate of true bifurcation lesions in the present study by Pan et al is substantial, and the operators should be congratulated on having included so many patients with advanced bifurcation disease.

Long-term data from the bifurcation subsets of large “most-comer” and “all-comer” DES studies may be of additional interest, as they generally include all types of bifurcation lesions treated in real-world clinical practice, including bifurcation lesions that right from the beginning of the percutaneous coronary intervention procedure are intended to be treated with a 2-stent approach. While some large DES trials have already reported detailed information on the outcome of their bifurcation subsets,\textsuperscript{4,5} others have yet to report such data.\textsuperscript{14,19}

There is also good reason to assess very carefully the subset of patients with bifurcation treatment in studies that examine bioresorbable vascular scaffolds. Current polymer-based vascular scaffolds bear the risk of being disrupted from post-dilatation with an oversized balloon, as is quite often performed in long metal stents to accommodate the stent to vessel tapering, which is particularly pronounced in coronary segments with major bifurcations.\textsuperscript{19} Moreover, simultaneous kissing balloon inflation in polymer-based bioresorbable vascular scaffolds bears the risk of disrupting struts of the scaffold and should therefore only be performed in cases in which it is absolutely deemed necessary.\textsuperscript{19} A modified kissing balloon technique may be considered as an intermediate step, if sequential inflation of noncompliant balloons in side branch and main vessel fail to achieve a satisfactory result. This technique, which has been assessed in bench tests, first inflates the balloon in the side branch and then partially deflates that balloon, which is kept in place during the final balloon dilatation in the main vessel.\textsuperscript{19} Hence, in the setting of bifurcation treatment with bioresorbable vascular scaffolds, further bench testing and computer modeling as well as clinical studies with optical coherence tomography are of interest. Moreover, the fate of side branches that are (initially) partially covered by struts of bioresorbable scaffolds should be carefully assessed, including long-term studies with optical coherence tomography. While currently only a few biodegradable vascular scaffolds are available, a number of companies may launch novel bioresorbable devices before long. Among other measures, the performance of these implants in bifurcation lesions will be an important criterion for selection and may help sort out less suitable devices.

In conclusion, bifurcation lesions are still a serious touchstone of novel DES and biodegradable vascular scaffolds. The assessment of outcome following percutaneous coronary intervention in bifurcations is an issue of ongoing scientific and clinical interest.

**CONFLICTS OF INTEREST**

Clemens von Birgelen is or has been consultant to and has received lecture fees or travel expenses from Abbott Vascular, Boston Scientific, and Medtronic; he received travel expenses from Biotronik and lecture fees from MSD; the institution has received research grants from Abbott Vascular, Biotronik, Boston Scientific, and Medtronic. All other authors declare that they have no further conflict of interest.

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