We would like to thank Dr. Saito for his interest in our study (1) evaluating the influence of a downstream epicardial stenosis on the fractional flow reserve measurement of an intermediate left main stenosis with the pressure wire positioned in the nondiseased contralateral vessel. We agree with Dr. Saito that the findings are in accordance with mathematical equations like the one he proposes and the one we have previously published, which demonstrated our understanding of the background mechanism (2). Unfortunately, these equations and the even more complex one proposed for the case in which both downstream vessels are diseased suffer from the major limitation that they assume the microvascular resistance in each downstream vessel. Moreover, as was the case with the equations proposed for evaluating the individual fractional flow reserve values of serial stenoses (3,4), their complexity makes it unlikely that a practicing interventional cardiologist will apply them clinically. We are pleased that Dr. Saito’s letter highlights the practical message of our paper, that the effect of downstream epicardial disease on the functional assessment of intermediate left main disease with the pressure wire in the non-diseased downstream epicardial vessel is small and clinically irrelevant, unless the downstream disease is severe.

REFERENCES

The Role of Drug-Eluting Balloons in Bifurcations
The Remaining Variable to Fit the Perfect Equation

We have read with great interest and satisfaction the elegant paper written by Kim et al. (1) and the editorial by Abdel-Latif et al. (2); we want to congratulate the authors on the original design of these 2 trials. As occurs with chronic total occlusions and left main disease, bifurcation lesions represent a constantly debated issue in all the meetings of Interventional Cardiology, and despite the large number of trials and the different techniques tested, there still exist unresolved aspects in the treatment of this subset of patients. To date, none of the dedicated stent platforms has shown relevant advantages over the conventional drug-eluting stents (DES) because of their higher profile, the complexity of utilization, or the need for additional stents, and although there is a general agreement supported by previous trials that provisional stenting is the best choice, there is still significant heterogeneity, and different techniques are widely used, such as crush, T-stenting, modified T-stenting, culotte, and a large list of the mentioned dedicated stents and techniques. The data provided by these 2 trials with 54% of second-generation DES in the CROSS (Choice Of Optimal Strategy For Bifurcation Lesions With Normal Side Branch) and 37% in the PERFECT (Optimal Stenting Strategy For True Bifurcation Lesions) trials show us the best paths to face against these challenging lesions in the following years. Second-generation stents have...
clearly modified the rules of the game on the basis of their better results, drawing the meaningful conclusion that the treatment of bifurcation lesions has become a much easier procedure because, seemingly, the complex strategies add no advantages over provisional stenting, and the role of a previously considered mandatory technique, despite being technically demanding, that is, the final kissing balloon inflation, nowadays is only necessary in selected cases. Moreover, there are also reasons for the optimism because there may exist room for improvement because the third-generation DES without polymer or with biodegradable ones may behave even better. In our opinion, we are really close to reaching the perfect knowledge in the treatment of bifurcations. However, we believe that one remaining question is still unanswered: previous reports have demonstrated the ability of drug-eluting balloons to diminish the restenosis rate in the origin of the side branch (3,4), which is the Achilles’ heel of these lesions. With the background information provided by the CROSS and PERFECT studies in hand, we believe that the only remaining question would be to clarify whether drug-eluting balloons might enable a reduction in the already low rate of major adverse cardiac events found in these trials. Once this last question is resolved, their treatment will be faced with less heterogeneity, and bifurcations will not represent a pending issue in future meetings.

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**REFERENCES**


**REPLY: The Role of Drug-Eluting Balloons in Bifurcations: The Remaining Variable to Fit the Perfect Equation**

We thank Dr. Lozano and colleagues for their interest in our study (1). The CROSS and PERFECT studies showed that any bifurcation stenting technique can yield a good clinical outcome once the procedure is optimally performed using intravascular ultrasound and new-generation drug-eluting stents (DES) (1). However, routine use of final kissing balloon inflation or the double-stent technique cannot contribute to good clinical outcomes, potentially leading to unfavorable angiographic outcomes. Therefore, our study emphasized that the most important aspect of bifurcation stenting is to perform the optimal procedure using a new-generation DES and not the selection of a bifurcation stenting technique. Moreover, our study results indicate that judgment of whether each side branch (SB) should or should not be treated must be made very judiciously. Given the ischemic threshold reported by Hachamovitch et al. (2), above which revascularization leads to a survival benefit, SB without functional significance does not need to be revascularized unless the blood flow is compromised.

As indicated by Loh and Waksman (3), a drug-coated balloon (DCB) may be used as an alternative to conventional SB treatment. Despite the lack of evidence, a DCB may be helpful for preventing intimal growth caused by balloon injury without any additional DES implantation. Nonetheless, there are several prerequisites for DCBs to be used for SB revascularization. Practically, DCBs of various sizes should be developed to fit a small SB. A recrossing technique to minimize drug denudation should also be investigated. Importantly, clinical evidence to support the benefit of DCBs for native vessels should be accumulated. For now, DCBs are qualified as a reliable option for revascularization of in-stent restenosis (ISR) following bifurcation stenting (4). Added to the previously implanted stents, repeatedly implanted DES for bifurcation ISR lesions lead to excessive stent layers, especially after using the double-stent technique. However, DCB can prevent neointimal hyperplasia with an antiproliferative drug without additional stent implantation.

In conclusion, the functional evaluation of SB is of paramount importance before determining its revascularization. Once this is decided, stent optimization