**LETTERS TO THE EDITOR**

**Tissue Sirolimus Levels of Distal Vessel, Stented Myocardium, and Distal Myocardium**

With great interest we read the article by Li et al. (1) regarding vasomotor functional responses of a conduit coronary artery distal to sirolimus-eluting stents in a porcine model. The researchers stated in the discussion, “...most of the drug taken up into cardiac tissue was transferred by direct contact with the arterial wall, which may have served as a reservoir for subsequent transfer via diffusion, or the vasa vasorum” (1). However, we have previously reported that tissue sirolimus levels of proximal/distal vessel, stented myocardium, and proximal/distal myocardium were much lower (less than 2%) than the stented vessel area concentration (peaked at 1 day after stent implantation [14.5 ± 10.9 ng/ml]). Moreover, sirolimus was not detected in either the proximal or distal myocardium at 30 days(2). Therefore, even low sirolimus concentrations with short duration may affect vasomotor function.

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doi:10.1016/j.jcin.2008.08.005

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**What We Should Know About Bifurcation Disease**

I read with great interest the paper by Latib and Colombo (1). This review discussed 6 major classifications of coronary bifurcation lesions. However, it failed to include a recently published comprehensive classification of bifurcation lesions that is simple, practical, and inclusive of other important features of coronary bifurcation lesions that are not mentioned in other classifications (2). This classification is based on a system composed of a single prefix (B, for bifurcation lesion) to which up to 3 main suffixes are added, describing important anatomical features of a given bifurcation lesion. This classification addresses 3 important technical features of bifurcation lesions: the proximal segment size, atherosclerotic disease burden, and the bifurcation angle. It is known that if the proximal segment is too small (small is defined as less than two-thirds of the sum of the diameters of both branch vessels [suffix S, for small]), the kissing stenting technique cannot be utilized (3). The Medina classification does not include this

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The observations of Dr. Kaneda and colleagues are clearly pertinent to the issues we raised in the Discussion section of our article (1). A common hypothesis generated by both of our results seems to be whether long-term (1 month post-implantation of sirolimus-eluting stents [SES] and even later) vasomotor dysfunction might be caused by a direct effect of the drug itself at very low concentration or secondary effects mediated through SES-triggered cellular interactions (for example, chronic SES-induced inflammation in the stented segment elaborating cytokines or other substances that impact endothelium-dependent relaxation). We suggest that the data currently available are inconclusive, because neither of these possibilities can yet be ruled out. Of interest however is that Jabs et al. (2) recently reported increased superoxide and p67(phox)/rac1 nicotinamide adenine dinucleotide phosphate oxidase and reduced nitric oxide, along with vasomotor dysfunction, in the aortas of rats given a 1-week continuous infusion of sirolimus. Their report did not include a histological assessment, but the recruitment of inflammatory cells would seem to be a plausible potential mechanism underlying these phenomena.

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doi:10.1016/j.jcin.2008.08.006

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important anatomical feature, and this review did not mention this important feature.

The second suffix describes the involvement of the disease area of the bifurcation branches, namely, if both ostia at the bifurcation site are involved, the number “2” is used; if the main branch only is involved, “1m” is used; and if the side branch only is involved, “1s” is used. A B2 lesion in this classification is a true bifurcation lesion based on the Latib and Colombo (1) algorithmic approach to bifurcation intervention in their review. The labeling of B2 lesions would include 1.1.1, 1.0.1, and 0.1.1 in the Medina classification. As one can see, the Medina classification is more complicated in regard to true bifurcation lesions.

It is interesting to note that Latib and Colombo (1) did not include the Medina classification in their algorithmic approach to interventional techniques, although they referred to it as the preferred classification. Some other publications that used the Medina classification for simplicity also did not use it in their technical decision making, calling into question the clinical applicability of the Medina classification.

The bifurcation angle is another important feature of bifurcation lesions that is not mentioned in the Medina classification or in this review (1). Steep angulations have been found to be associated with higher risk for abrupt vessel closure (4), side branch occlusion (5), and major adverse cardiac events (6). In the Movahed classification, a third suffix describes the angulation of bifurcation branches. The suffix V is for angles of less than 70°, and the suffix T is for angles of more than 70°. A comparison of known classifications, including the Movahed classification with a detailed algorithmic approach to coronary bifurcation interventions based on the Movahed classification was recently published (7) as a guide to interventional cardiologists for technical decision making based on the lesion characteristics.

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doi:10.1016/j.jcin.2008.08.003

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Reply

We appreciate Dr. Movahed’s interest in our review (1). The 6 bifurcation classifications referenced in our review (2–7) were developed to allow researchers and clinicians to describe in a standardized way the distribution of plaque at the bifurcation. As can be seen from Figure 1 (8), all 6 describe the distribution of plaque in the 3 limbs of a bifurcation in a similar way and are thus easily comparable. The reason for our choice to emphasize the use of the Medina et al. (7) classification is that it does not require the interventionalist to commit to memory a complex mnemonic (9) to describe a bifurcation lesion and it gives the reader an immediate mental picture of the distribution of plaque at the bifurcation. We are pleased to see that our decision to emphasize the Medina classification is supported by Louvard et al. (10) of the European Bifurcation Club who have attempted to provide the first consensus document on bifurcation classifications, which states: “The classification by Medina et al. (7) is straightforward and does not need to be memorized even though it provides all the information contained in the others.” Despite these refinements, all current classifications have inherent limitations. Importantly, they do not describe a number of anatomical features that will influence and affect the interventional approach to a bifurcation lesion, such as extent and length of disease on the side branch (limited to the ostium or involving the vessel beyond the ostium), its size (≥2.5 mm of reference diameter) and distribution, and the angle between the main and side branches (1). All of these factors are essential and need to be documented, but their inclusion in a bifurcation classification would again increase the complexity of the classification and limit is clinical utility. Thus we would echo the words of Medina et al. (7) that the main purpose of a bifurcation classification is that it “allows for homogenous terminology when comparing different series and techniques” (7). The further issue relates to whether a bifurcation classification can predict outcomes or determine the interventional approach. A major part of the complexity of treating bifurcations arises from the fact that bifurcations vary not only in anatomy (plaque burden, location of plaque, angle between branches, diameter of branches, bifurcation site) but also in the dynamic changes that occur during the procedure, such as plaque shift and dissection. As a result, no 2 bifurcations are identical and there is no single strategy that can be applied to every bifurcation. For all these reasons we are relatively skeptical about the value of adding another classification system for bifurcation lesions. Nevertheless, the letter by Dr. Movahed has given an opportunity, for the interest of the reader, to look into a new descriptive way of classifying bifurcations. Only experience...