# Bifurcation Lesions: The Last Great Frontier for Coronary Interventions

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Atherosclerosis is a systemic disease that diffusely, although not uniformly, affects the arterial territory. Arterial bifurcations, due to the blood flow turbulence originating there, are the site of high endothelial stress that characteristically falls victim to atherosclerosis. Although there are many definitions of what constitutes a bifurcated lesion, from the perspective of coronary intervention it is accepted that it is the lesion that occurs adjacent to the origin of a secondary branch or that compromises this, and is significant in caliber and development. Some 10%-15% of lesions treated by angioplasty affect a bifurcation (unpublished data from Hospital de Alcorcón). For the interventional cardiologist, these lesions constitute a special difficulty, with worse immediate and midterm results.[1-3] Despite the fact we have celebrated the 30th anniversary of the birth of coronary intervention, the optimal approach to bifurcation lesions remains controversial and research into this issue continues.

## Bifurcation Morphology

The morphology of bifurcations is complex and varies greatly, making them extremely difficult to classify. Many variables influence the approach to and results of bifurcation lesions. These include: the site, severity and length of lesions, the position of plaque (contralateral or ipsilateral) in the main vessel (MV) with respect to the origin of the secondary branch (SB) and vice versa, the degree of calcification of the lesions, plaque load, MV and SB diameters, the angle of origin of the SB with respect to the MV, TIMI flow in each of the distal vessels. Moreover, lesions affecting the left coronary artery, or trifurcations, when no single vessel is clearly secondary, should probably be considered separate categories in their own right.

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Many classification systems have been described, which emphasizes the difficulty of describing this type of lesion. Currently, the most widely-used systems are Medina et al[4] and Lefreve et al.[5] Most classifications center on the variable site of the lesion in the MV with respect to the origin of the SB, and on whether or not the SB ostium is affected. More recently, the European Bifurcation Club has proposed a consensus nomenclature[5] based on the classification of Spanish researcher Dr Alfonso Medina. Its success lies in its simplicity: lesions are scored 0 or 1 depending on whether there is a lesion >50% in any of the 3 segments evaluated: immediately proximal, distal, and at the origin of the branch. If there is a lesion in any of these segments, it is scored 1 in this order of segments. Thus, if there were a lesion in the 3 segments, this would be classified as 1,1,1.

Clearly, we cannot ignore the fact that, to simplify the proposed classification, not all of the variables previously mentioned are covered, and many of these directly influence results.[6,7] For example, take the angle of the SB with respect to the MV. If this is <70º (Y morphology), access to this branch for the intervention will be greater but the chances of branch deterioration on inflating the balloon in the other vessel will also be greater due to plaque displacement. If the angle is >70º (T morphology), plaque displacement is less problematic but access to the branch can be more difficult should an intervention be needed. Finally, we must remember that the coronary vasculature is considered a fractal geometric object, governed by Murray's law,[8] and a relation exists between the main proximal vessel diameter and distal vessel diameters. The main proximal vessel diameter would be 0.67 times the sum of the main distal vessel and SB diameters. This demonstrates the difficulty of achieving adequate stent expansion in the proximal and distal segments using the simple technique of a single stent mounted on a balloon with a uniform diameter along its length. Finally, the difficulty of evaluating the severity of ostial and bifurcation lesions by angiography is well-known. Studies using fractional flow reserve have shown we frequently overestimate lesion severity in these circumstances, underlining the value of an additional evaluation technique to complement angiography in this context.[9]

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## Interventionist Approach to Bifurcation Lesions

### *Intervention Techniques. Classification*

Although interventional cardiologists have demonstrated notable imagination and proposed dozens of techniques for approaching bifurcations, little has been done to classify these. In 2008, European experts led by Dr Yves Louvard and including Dr Manuel Pan and Dr Alfonso Medina—coauthors of the article published in the present issue of *Revista Española de Cardiología*—proposed a classification intended to be both simple and exhaustive.[10] Under the appropriate acronym of MADS (MADS: Main, Across, Distal, Side) they gather techniques into 4 major groups depending on in which arterial segment (proximal, across the SB, distal, or SB) a first stent is implanted. Suffice it to say that more than 30 different techniques, detailed descriptions of which go beyond the purposes of this editorial, are currently in use.

The most simple approach to a bifurcation lesion consists of implanting a single stent in the MV across the SB, with only one stent implanted in the case of marked deterioration (the provisional stent in SB strategy). The main disadvantage of this approach is that it fails to resolve one of the most important problems in treating bifurcations—namely inadequate treatment of the SB ostium if this is diseased—and this is precisely where the acute result is worse and restenosis, greater.[3,11] The proliferation of 2-stent implant techniques, with one in the main vessel and the other in the secondary branch, has sought to resolve these problems. However, although aesthetically more satisfactory, they complicate the procedure substantially and have their own limitations, fundamentally derived from the difficulty of adequately covering all of the vessel between the 2 stents, or stent distortion, or the excess of metal that can remain in the carina of the bifurcation. In fact, these last 2 characteristics have also been associated with greater need for revascularization and with stent thrombosis.[3]

### *Conventional Stents or Drug-Eluting Stents (DES)? One Stent or 2?*

The 2-stent strategy (in MV and SB), using the platform of non-drug-eluting stents, has been practically abandoned due to clinical results worse than for provisional SB stenting,[1,12] with reported rates of restenosis of up to 62%.[1] The era of the DES led to renewed interest in the chance of improving the results of percutaneous treatment of bifurcations. Several randomized trials report results of comparing 1- and 2-DES strategies. In a study of 85 patients treated with sirolimus-eluting stents,[3] Colombo et al pointed to a trend toward greater rates of restenosis (28% vs 18.7%; $P$=.053) and thrombosis (3.5% vs 0%) in patients receiving 2 stents. In a study of 91 patients treated with sirolimus-eluting stents,[13] Pan et al found no differences in clinical events between patients receiving 1 versus those receiving 2 stents, although incidence of restenosis both in MV and in SB was numerically higher in the 2-stent group (MV and SB). The largest published trial is NORDIC,[14] with 413 patients randomized to 1 provisional sirolimus-eluting stent in SB or 2 sirolimus-eluting stents (MV and SB). Incidence of major clinical cardiac events was no different between one group and the other, but incidence of creatine kinase MB fraction (CK-MB) elevation >3-fold greater than normal was more frequent in the 3-stent group (18% vs 8%; $P$<.011). Incidence of stent thrombosis was low in both groups (0% and 0.5% respectively). Finally, incidence of MV restenosis was low in both groups (4.6% vs 5.1%), with a trend towards lower incidence of SB restenosis in the 2-stent group (11.5% vs 19.2%; $P$=.062). To summarize, accepting an initially complex access strategy did not lead to better clinical results, although it did not clearly impinge on results either, as occurred with uncovered stents. These results indicate the provisional SB stent strategy has gained acceptance as the most prevalent in most cardiac catheterization laboratories. Even so, contexts exist which necessitate stent implantation in the 2 branches, as occurs in lesions in which the SB is larger and presents a greater load of plaque, fundamentally if the lesion is large, as well as when marked SB deterioration occurs on treating the MV or when the angle of origin of the SB with respect to the MV makes further access to this artery complicated.

### *The Problem of Stent Distortion Following SB Dilatation*

One important practical consideration is that, once a stent has been implanted in the MV, SB dilatation invariably distorts MV stent structure, as in vitro studies have clearly shown.[15] Consequently, generally accepted practice is to inflate balloons simultaneously in both branches if SB is dilated. It is precisely the in vivo evaluation of the mechanics of MV stent distortion following SB dilatation that constitutes the objective of Suárez de Lezo et al's article[16] in the present issue of the *Revista Española de Cardiología*. Using intracoronary ultrasound in a study of 23 patients, the authors show the harmful effect that SB balloon inflation has on lumen dimensions of the MV stent in the segment immediately distal to the origin of the branch. The authors, who have made important contributions to the bifurcation lesion treatment, present data indicating that even simultaneous dilatation in both branches fails to recover initial lumen. This is of particular importance as stent lumen dimensions are directly related with the chances of restenosis occurring and influence the appearance of thrombosis. However, we must say that many anatomic variables can influence results, as mentioned above, and important aspects of the procedure, such as balloon size and pressure, as well as technique type in 2-stent interventions, also influence final results.[17]

The use of a simple strategy with implantation of one stent in the MV produces good results in a large proportion of patients. Consequently, the dominant strategy in bifurcated lesion treatment is currently that of the provisional stent in the SB. However, active research into the treatment of bifurcations continues and is of particular interest to interventional cardiologists. Research techniques that are more sensitive than angiography—such as intracoronary ultrasound in the study discussed here, or optical coherence tomography—provide data that permit improved results. Although the initial 1-stent strategy is preferred, a considerable percentage of lesions finally need 2-stent implants due to inadequate results in the SB and therefore, as a minimum, we need to define a safe, reliable approach so the procedure can be changed to allow for 2-stent implants with adequate expansion of this and complete coverage of the SB ostium. In this context, a whole series of DES specifically designed to treat bifurcations are waiting in the wings for evaluation in the clinical arena. The use of detailed classifications will help us learn and compare techniques and devices to find those better suited to the very different anatomic features the coronary vasculature offers us.

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