

Drug-eluting stents: the equalizers in treatment of bifurcational lesions

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We have in this inaugural issue of the Journal two interesting papers relating to the stenting of bifurcational lesions. The reader needs to examine firstly the report of Lefèvre et al, and hence read the following from Hoye et al. In these two studies, we see the evolution of coronary stenting for bifurcational lesions due to the introduction of drug-eluting stents (DES). What was considered problematic, (the stenting technique utilizing two stents) in the study of Lefèvre, becomes inconsequential in the report of Hoye utilizing drug-eluting stents.

The first study has the major value of enrolling 1149 patients. The type of bifurcations treated varies and includes lesions where the disease is limited to the main branch. The authors used as a default strategy to stent only the main branch and utilization of two stents, mainly with the T approach, was used as a provisional alternative and rarely as an intention to treat solution. This approach led to stenting the side branch in only 30% of the cases while the main branch was always stented. In 7% of the patients there was no angiographic success in the side branch. Almost all patients were followed for at least 6 months and the overall incidence of major adverse cardiac events (MACE) was 18.1%: death 1.6%, myocardial infarction and death 5.5%, target vessel revascularization (TVR) 13.2%. Multivariate analysis showed that implantation of 2 stents (main and side branch) was a predictor for MACE during follow-up. Few important elements need to be considered: the deployment of bare metal stents, the absence of systematic angiographic follow-up, and the fact that the operator chose the double stenting approach in conditions evaluated not ideal for one stent or in which a single stent on the main branch gave a suboptimal result. The deployment of two bare metal stents is a well known strategy to be associated with high event rates in bifurcational lesions^{1,2}. The lack of systematic angiographic follow-up will contribute to lower the need for TVR³, in particular for the side branch. Furthermore, it is not rare for patients with angiographic restenosis of the side branch to be asymptomatic^{1,2,4}. The fact that the operator using the single stent technique as a default approach, implanted in some lesions

two stents is very likely to point out that the lesions treated with two stents were the most complex, and therefore the ones associated with a less favorable outcome^{4,7}. The questions that remain without a clear answer are the following: to what extent implanting two stents acts as a marker of disease and to what extent does this strategy contribute to a higher restenosis rate and need for TVR? As in most of these situations I think that both factors contribute to generate MACE.

To our rescue DES has become available^{4,8,9}. The study of Hoye et al. explores the outcome following implantation of sirolimus eluting stents (SES) in 144 patients and paclitaxel eluting stents (PES) in 104 patients. This study is much smaller in sample size compared to the previous one, but has a unique value since it is almost a mirror image of the report by Lefèvre et al. Contrary to the first study, Hoye et al used the two stent approach in about 80% of the patients. When two stents were used, T stenting and Crush were the techniques most frequently employed. Also, Hoye et al reported a more liberal administration of IIb/IIIa inhibitors and used in about 30% of the patients in comparison to the first study. Except for a larger reference vessel diameter of the main branch and a longer stent length implanted in the side branch of the PES group, there were no major differences in the baseline characteristics between patients treated with SES or PES. Similarly to the previous study, angiographic follow-up was not actively sought and it is not reported in the findings. Stent thrombosis was angiographically demonstrated in 2 patients treated with SES (1.4%) and in 3 patients treated with PES (2.9%). At 6 months, 96.7% of the patients treated with SES and 86.8% of the ones treated with PES were free from target lesion revascularization (TLR)($P=0.01$). In more detail, the breakdown of TLR was subacute thrombosis (see above) for 5 cases, restenosis of the main vessel for 10 lesions [4 treated with SES (2.4%) and 6 treated with PES (5.3%)], restenosis of the side branch for 6 lesions [3 treated with SES (1.8%) and 3 treated with PES (2.7%)], and restenosis of both branches for 4 lesions [2 treated with SES (1.2%) and 2 treated with PES (1.8%)].

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The important findings of the work of Hoye et al. are that the technical approach utilised to treat the bifurcation did not appear associated with the outcome. We cannot dismiss the fact that this study did not include angiographic follow-up and many focal restenosis involving the side branch could have been missed. This limitation is however present also in the first study. The conclusion we can reach when we put the two studies side by side is that the introduction of DES became the equalising factor. How does this message translate into clinical practice: If you need to use one stent it is always better and cheaper, if you need two stents do not think you will be penalised in the outcome. Of course the stents must be DES!

Recently, we reported a rate of 3.6% of cumulative stent thrombosis after DES implantation in bifurcations in a prospective observational cohort study which included 2229 patients treated with both SES (n=1062) and PES (n=1167)¹⁰. In this study, bifurcation lesion treatment was identified as independent predictor of subacute (post-procedure to 30 days), late (>30 days), and cumulative thrombosis. However, there were no significant differences regarding the incidence of thrombosis in bifurcations treated with one versus two stents¹⁰. Similarly to the above report, Hoye et al found a numerical difference regarding the incidence of stent thrombosis between the 2 groups. However, this difference did not reach any statistical significance. More specifically, angiographically documented stent thrombosis occurred in 2 patients treated with SES (1.4%) and 3 patients treated with PES (2.9%), p=0.4. At 6-months, the survival-free of TLR rate was 95.7% for SES versus 86.8% for PES, p=0.01. These findings may be provocative and may attract further conclusions. We would like to take this opportunity to downplay these results and remind the reader that such a profound statement and conclusions can only come from a prospective, well powered randomized study.

Big conclusions need big studies with big numbers.

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