Drug-Eluting Stent Safety - Is It Time to Turn the Page on Barcelona 2006?

Written by Maria Vinall

While it is generally agreed that drug-eluting stents (DES) can dramatically reduce the need for revascularization, many believe that the issue remains as to whether the late thrombosis that is seen with DES results in an increase in myocardial infarction (MI) and death. Professor Edoardo Camenzind, MD, University Hospital, Geneva, Switzerland, said that "to understand the literature, DES articles need to be scrutinized to reveal their essence." Based on his own review of the literature, he does not believe that the concerns about the clinical impact of late stent thrombosis can be "definitely dissipated."

Prof. Camenzind provided two examples. In the first, he compared the Landmark analysis (6-month vs long-term follow-up) of the 2003 and 2004 patient cohort of the SCAAR (Swedish Coronary Angiography and Angioplasty Registry) registry [Lagerqvist B et al. *New Engl J Med* 2007], which showed a significantly increased long-term rate of death/MI with DES versus bare metal stents (BMS), with the recently published 2003 to 2006 patient cohort, which showed similar rates of death/MI between the two stent types [James SK et al. *New Engl J Med* 2009]. After reviewing the data, Prof. Camenzind suggested that the change in rates of death/MI between the two types of stents in the newer study may not be associated with better DES outcomes over the longer follow-up. Instead, he hypothesized, they may be due to the worse 'early' (within the first 6 months) outcomes for BMS in the 2005 and 2006 patient cohort of the registry, which was associated with a higher number of patients with ST-segment elevation myocardial infarction (STEMI) in the BMS group versus the DES group during that period. Thus, the imbalanced indication, not the stent type, may drive the outcome in the latest SCAAR registry results. In his second example, Prof. Camenzind commented on the results of a 2007 meta-analysis that also showed a similar mortality risk with DES and BMS [Stettler C et al. *Lancet* 2007]. After reviewing the data, Prof. Camenzind noted that 44% of the data in this analysis were derived from DES-versus-DES trials and not BMS-versus-DES trials. "The data are not really comparable," he said, and further, none of the long-term data (>1 year) were referenced in the paper, in contrast to the data that were presented in 2006 in Barcelona [Camenzind E et al. *Circulation* 2007].

Taking a different view, Professor Adnan Kastrati, MD, Deutches Herzzentrum, Munich, Germany, began by stating that "DES are the most successful therapy to date for prevention of restenosis, and these benefits are not achieved at the expense of compromised safety." He reviewed some of the meta-analyses that showed the efficacy and safety of DES [Kastrati A, Schömig A. *J Am Coll Cardiol* 2007; Kirtane AJ et al. *Circulation* 2009], even in patients with diabetes [Stettler C et al. *Br Med J* 2008] and STEMI [Brar SS et al. *J Am Coll Cardiol* 2009]. Commenting on several head-to-head studies that used different stents [Schömig A et al. *J Am Coll Cardiol* 2007; Park SJ et al. ACC 2009; Serruys P et al. ACC 2009], Prof. Kastrati noted that not all DES are equal and that the differences between the various DES and the emergence of stents that are based on biodegradable polymers indicate that there is still room to improve the technology.

Professor Stefan James, MD, Uppsala University Hospital, Uppsala, Sweden, shared unpublished data from the SCAAR registry, showing that for the population of subjects who were enrolled between 2003 and 2004 and followed for up to 5 years, the relative risk of death/MI that was associated with DES remained unchanged from the originally reported 3-year data (RR, 1.2), suggesting that the risk could not be explained by the continuing enrollment or length of follow-up. Prof. James also presented 6-year data from SCAAR that included 60,937 patients who were enrolled between 2003 and 2007 that showed no difference in the risk of death/MI (RR, 1.00) or death alone (RR, 0.96) between the BMS and DES patients. "These data, in conjunction with reassuring data from long term follow-ups in large registries with high-risk patients, such as those with STEMI [Mauri et al. *N Engl J Med* 2008] and diabetes [Garg et al. *Circulation* 2008], provide the impetus to 'turn the page' on Barcelona 2006 and begin to evaluate new types of DES, such as those with bioabsorbable polymers and stent struts, and to define the role of more potent antithrombotic treatments and their duration," said Prof. James. Still, we need to be aware of the infrequent but increased risk of late-occurring stent thrombosis with the first-generation DES, make sure to select patients who are likely to comply with long-term dual antiplatelet therapy, and optimize the implantation technique.

In closing the session, David R. Holmes, MD, Mayo Clinic, Rochester, MN, stated, "It is undoubtedly true that DES reduce clinical and angiographic restenosis significantly, but they are not a panacea for prevention of all cardiovascular events." Dr. Holmes recommended careful attention to the issues of optimal antiplatelet therapy, noting that new strategies of care continue to evolve, such as platelet function testing and new adjunctive medical therapy regimens.