Re-evaluating Stents: Objective Data from Large Patient Registries

CHICAGO - New data presented in recent months as well as a new meta-analysis continue to suggest that drug-eluting stents (DES) are superior to bare metal stents (BMS) for long-term outcomes in most settings. At the 2008 scientific sessions of the Society for Cardiovascular Angiography and Interventions (held in conjunction with the American College of Cardiology), data from four registries evaluating stents in several different types of populations generated the same conclusion that was produced by two recently published studies. Whether employed for on- or off-label indications, DES performs as well or better than BMS, typically yielding a mortality advantage. The largest of the registries presented at the SCAI meeting evaluated DES following acute myocardial infarction. The unadjusted absolute mortality at the end of two years was 5% lower in the DES group than in BMS patients (9% vs. 14%; \(P<0.001\)). These benefits were still observed after adjustment for risk factors, such as diabetes. Risk-adjusted relative mortality rates of 10.6% were seen in the DES group vs. 13.4% in the BMS group (\(P=0.002\)).

Seven new sets of data, including five presented at the annual SCAI meeting, evaluate a population not included in earlier studies comparing DES to BMS. While the number of patients who received DES was slightly higher than the number who received BMS (4016 vs. 3200), matched pairs were employed for an adjusted analysis. The data presented were on 1221 matched pairs of STEMI patients and 1322 matched pairs of non-STEMI patients.

All outcomes favoured DES over BMS. For the population as a whole, DES were associated with a 2.7% reduction in death (\(P=0.002\)) at two years. For STEMI patients, the mortality reduction was 3.1% (\(P=0.009\)). In non-STEMI patients, there was a 1.9% reduction for DES over BMS, but this did not reach statistical significance (\(P=0.18\)). There was a 5.3% reduction in revascularizations for DES relative to BMS for all patients, for STEMI patients and for non-STEMI patients (\(P<0.001\) for each comparison). Although recurrent MI rates were lower for DES relative to BMS overall as well as in STEMI and non-STEMI patients, all differences fell short of statistical significance (\(P=0.08\) for all patients).

“The previous data on DES in acute MI have been limited. These results suggest that DES do not increase risk relative to BMS in acute MI but appear to improve long-term outcome,” Dr. Mauri indicated.

In a multicentre European study comparing outcomes in 913 patients who received a DES and 2105 who received a
BMS, two-year mortality was lower in the DES group overall (2.0% vs. 4.1%; \(P=0.003\)) and after patient matching (1.8% vs. 4.0%; \(P=0.01\)). The mortality benefit was observed despite the fact that DES patients were more likely to be diabetic (\(P<0.001\)) and have off-label lesion types, such as long lesions or lesions in small vessels (\(P<0.001\)).

According to Dr. Albert E. Alahmar, Cardiothoracic Centre, Liverpool University, UK, “Long-term mortality following DES has been raised as a concern, but in our real-world setting, DES were associated with lower mortality relative to BMS despite some potential disadvantages for the DES group in terms of baseline risk.”

A similar conclusion was drawn by Dr. Dmitriy N. Feldman, Weill Cornell Medical College, New York, New York, who presented data on 2174 patients who underwent DES implantation and 188 who received a BMS. With a mean follow-up of 24.8 months, mortality was 4% in the DES group vs. 13.8% in the BMS group (\(P<0.001\)).

After multivariate Cox analysis, DES were associated with a 60% improvement in long-term survival (HR 0.4, 95% CI 0.2 - 0.7; \(P=0.001\)).

“DES use in comparison with BMS is associated with improved in-hospital and long-term survival in real-world practice,” noted Dr. Feldman, who stressed that registry data might be more useful than prospective randomized trials in confirming the safety and efficacy of stent performance out of the hands of expert interventionists who participate in clinical trials.

**Off-label Data**

In addition to the AMI registry, one other registry and a meta-analysis presented at the SCAI meeting focused on off-label stenting. In the registry, 4002 consecutive patients received DES for such indications as STEMI, chronic total occlusion, bypass graft, in-stent restenosis, long lesions, and small vessel diameters. None of these indications were included in the original randomized trials of DES. When compared to BMS implanted for the same indications in a retrospective analysis of patients treated at the Cleveland Clinic, Ohio, DES were associated with a 47% reduction in mortality (HR - 0.53, 95% CI 0.42 - 0.67; \(P<0.0001\)). The 34% reduction in the rate of recurrent MIs in DES vs. BMS patients produced a trend (\(P=0.13\)). There were no differences in vessel revascularization rates.

“When used in an off-label setting, DES appear to perform at least as well, and possibly better, than BMS in similar lesions,” stated cardiologist Dr. John M. Galla, Cleveland Clinic.

In a meta-analysis conducted by another group of investigators, data were collated from six published registries comparing DES to BMS. The 1252 patients, who were followed between six and 24 months, were stratified in this analysis by treatment for left main lesions, saphenous vein graft lesions, ostial lesions and total occlusions. In those treated with DES, there was 76% overall reduction in the risk of target vessel revascularization at the end of six months relative to BMS (95% CI 0.12 - 0.45). Although the 40% reduction in mortality at the end of one to two years of following in DES vs. BMS patients (HR 0.60, 95% CI 0.27 - 1.129) did not reach statistical significance, there was also “no mortality hazard with the off-label use of DES compared to BMS for any lesion subtype evaluated,” according to Dr. Nirat Beohar, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

These results are consistent with the recently published study that analyzed data from 6551 patients in the National Heart, Lung, and Blood Institute Dynamic registry (Marroquin et al. *N Engl J Med* 2008;358:342-52). The goal was to compare DES to BMS for off-label use, defined as use in restenotic lesions, lesions in a bypass graft, left main coronary artery disease, or ostial bifurcated or totally occluded lesions (as well as in lesions >30 mm in length and lesions <2.5 mm or >3.75 mm). This study was specifically prompted by concerns about off-label use.

“Our study showed that the use of DES as compared with BMS was associated with a lower risk of repeat revascularization at one year of follow-up. This beneficial effect was achieved without any excess risk of death of MI,” reported a team of investigators led by Dr. Oscar C. Marroquin, Cardiovascular Institute, University of Pittsburgh, Pennsylvania.

In a report published just two weeks later by Applegate et al. (*JACC* 2008;51:607-14) that evaluated clinical outcomes in 1164 consecutive patients receiving off-label stent therapy, there was not only a 38% reduction (\(P<0.001\)) in target vessel revascularization in the DES vs. the BMS group at the end of two years, but DES was also associated with a 29% relative reduction in mortality (\(P=0.01\)).

**Summary**

In response to a previous series of conflicting reports, a large body of data has demonstrated long-term outcome advantages for DES over BMS in both on- and off-label indications for stent implantation. The newly presented data reinforce two recently published studies. The mortality advantage, which was significant in most but not all studies, reinforces the utility of DES including use for on- and off-label indications.