

DRUG-ELUTING STENT SOLUTIONS



Real-World Registry Data at TCT 2007

This monthly column in Cath Lab Digest reviews important points of distinction in drug-eluting stents (DES), from characteristics to techniques, so that physicians have valuable and relevant information about this revolutionary technology.

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Dr. Lasala received the Outstanding Cardiology Alumnus Award from Yale University School of Medicine in 2000, where he did his cardiology and interventional cardiology fellowships. Currently, Dr. Lasala is Associate Professor of Medicine, Washington University School of Medicine; Director of Interventional Cardiology and Medical Director of the Cardiac Catheterization Lab, Barnes-Jewish Hospital, St. Louis, Missouri. Dr. Lasala is the Primary Investigator for more than 30 research trials and the Co-Investigator for 13 studies, including ARRIVE. He has had more than 40 peer-reviewed manuscripts published and has various editorial responsibilities, including the *American Heart Journal*, *American Journal of Cardiology*, *Journal of American College of Cardiology*, *Circulation* and *Catheterization & Cardiovascular Intervention*. Special research interests include congenital heart disease and Stereotaxis.

Q What was your impression of this year's Transcatheter Cardiovascular Therapeutics (TCT) meeting?

A The overall atmosphere at TCT 2007 was much calmer than last year's meeting, buoyed by late follow-up analyses from the major trials and a wide range of stent registry reports. We saw more abundant data — single-center and multi-center studies, as well as regional studies from different geographic areas — so this year we had a much clearer picture of the current state of drug-eluting stents (DES), and there was less concern about some of the previously reported adverse event rates.

Q In a TCT 2007 presentation summarizing all of the trial and registry data to date, Dr. Gregg Stone (Columbia University) concluded that the bulk of the data are largely reassuring. Would you agree?

A Yes, I would agree with Dr. Stone's conclusion. The increasing number of cases included in large meta-analyses eliminates some of the sporadic, somewhat spurious, adverse events that the data alluded to earlier. What we see in standard practice when used within labeled indications are rates of mortality and myocardial infarction (MI) with DES being equal to (see Figure 1) — and in some cases even slightly lower than — rates with bare-metal stents (BMS).

It is important to remember that with low-frequency events such as very-late stent thrombosis, it is possible for rates to fluctuate quite dramatically. We have to base our conclusions on a much larger number of cases in a broader range of conditions.

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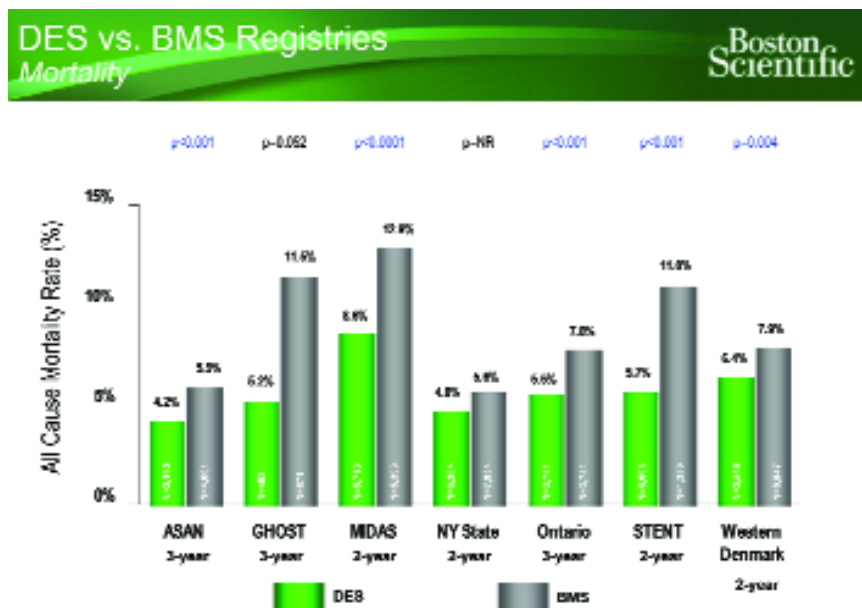


Figure 1. ASAN data presented by SJ Park, TCT 2007. GHOST data presented by Harjai, TCT 2007. MIDAS data presented by Vagonescu, TCT 2007. NY State data presented by Hannan, TCT 2007. Ontario data presented by Ko, TCT 2007. STENT data presented by Brodie, TCT 2007. Western Denmark data presented by Jensen, TCT 2007.

Q You make a good point. Double-blind randomized trials have shown that on-label use of DES does not increase overall death and MI rates. What is the important take-away for interventional cardiologists based on these data?

A There are three important take-away messages. First, DES clearly lower rates of restenosis by a factor of 50 to 70 percent. Interventionalists must keep these numbers in mind when reviewing the utilization of these stents. Second, when you look at the death or MI endpoints, there is no difference between DES and BMS. There has been some suggestion that there might be an increase in both of these endpoints with DES. However, there is no signal that this is true, based on thousands of patients in clinical trials. Third, very-late stent thrombosis does occur at a slightly increased frequency with DES compared to BMS, but rates of this event with DES are beginning to plateau in the most recent data from the two earliest of the blinded, randomized trials, TAXUS IV and SIRIUS. Rates of very-late stent thrombosis are less the second year compared to the first, and there is no additional very-late stent thrombosis beyond four years.

Q As you know, TCT 2007 featured updates on some of the registry studies that have been at the center of the stent thrombosis debate over the past year, including SCAAR. The four-year SCAAR data presented at TCT pointed to higher adverse-event rates in off-label vs. on-label DES use, but no overall increase in death or MI in DES compared to BMS-treated patients. What can be concluded from this data about stent thrombosis?

A The Swedish Coronary Angiography and Angioplasty Registry (SCAAR) points out the potential pitfalls of analyzing endpoints of relatively low frequency, particularly stent thrombosis. The four-year presentation at TCT suggests that rates have pretty much leveled off, and a signal is no longer seen. Again, people should realize that there is going to be some biological variation in this particular endpoint, particularly when it's a low number occurring at a low frequency and, to be accurate, it takes a large N that is followed for an extended period of time.

Q Is there anything else that these trials are telling us?

A DES have taught us many lessons, one of which is that the traditional six-month or one-year cut-off that we are used to following for stent registries and trials is no longer adequate. The most recent data from ARRIVE — which now includes almost 7,500 cases — shows that events are still occurring between years one and two. The slope of those events is considerably

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reduced in the second year compared to the first year, but the fact is that there are still some events taking place, so we've learned that one-year data is not enough. It looks like we need to follow patients at least two to three years and maybe even five years.

Q We saw five-year data from TAXUS IV at TCT. Any overall impressions based on that data?

A The improvement and efficacy of DES has been maintained both in the TAXUS IV five-year data and the SIRIUS data. These data show that DES have maintained the same advantage over BMS that we saw in the first year of the trials, and we've seen a complete flattening of the rate of very-late stent thrombosis with both the TAXUS Stent and CYPHER Stent.

Q Given the real-world registry data presented at TCT 2007, how should physicians now weigh the risks and benefits of DES vs. BMS?

A I think that the pendulum has swung as far back to the left as it needed, and now we can begin to use DES in a more educated, more sophisticated fashion. Now it's our job to educate our patients by discussing with them the risks and benefits. It's clear that people should not get a DES unless they can take a minimum of one year of dual anti-platelet therapy. In selected cases, this may extend to two or even three years. Interventionalists must determine what their patients are capable of doing. Are they reliable to take medications? Can they afford to take the medications? Are there any comorbidities or concomitant medical conditions that will prevent them or put them at risk for taking prolonged dual anti-platelet therapy?

From there, we need to focus on the future. We need to figure out how to prevent the relatively infrequent, but certainly worrisome, problem of very-late stent thrombosis. In order to be able to apply DES across the board, we need to come up with better technology – more rapidly healing DES, DES that endothelialize so they become biologically neutral, etc. Hopefully within the next decade, we'll be able to apply DES without any significant concerns for our patients in terms of very-late stent thrombosis and dual-antiplatelet therapy.

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