Most DESs Placed in Patients With Trial Exclusions

Those with risk factors outside of the trial criteria had worse outcomes and higher hospitalization costs.

BY MITCHEL L. ZOLER
Philadelphia Bureau

STOCKHOLM — Four-fifths of the more than 3,000 patients who received drug-eluting coronary stents at one U.S. medical center fell outside the entry criteria used in the major trials of such stents.

And patients with risk factors that placed them outside of the trial criteria had, in general, much worse outcomes than did patients who met the trial criteria. For example, patients with two high-risk factors that were not included in the original trials had an 11.3% rate of major adverse cardiac events (MACE) during the first year after receiving drug-eluting stents, double the 5.7% rate seen in patients who fell within the trial criteria, Gregory J. Mishkel, M.D., reported in a poster at the annual congress of the European Society of Cardiology. The cost of hospitalization also rose as the number of risk factors rose.

The findings raised the question of whether the use of drug-eluting stents is preferable to coronary bypass surgery in patients with several risk factors. "In patients with three or more risk factors, bypass remains a viable option," Dr. Mishkel said in an interview. The results from the randomized, controlled trials of drug-eluting coronary stents "do not directly translate to the real world," because in the real world patients have more risk factors, he added.

The study reviewed all 3,059 patients who received a drug-eluting coronary stent at St. John's Hospital in Springfield, Ill., during May 2003–December 2004. Among this group, 613 (20%) met enrollment criteria for either the RAVEL or SIRIUS trials, which were the major studies to test the safety and efficacy of sirolimus-eluting coronary stents (Cypher), or the TAXUS studies, which were the major studies to test paclitaxel-eluting stents (Taxus). All of the other patients had at least one factor that would have excluded them from these trials. These risk factors included multilesion stenting, a bifurcated lesion, and a vessel diameter of less than 2.5 mm. More than 10% of the St. John's patients had at least four high-risk factors.

The patients with no risk factors had the lowest incidence of MACE during the first year following stent placement. The MACE rate increased as the number of risk factors increased, rising to 8.2% in patients with any single risk factor, 13.7% in those with three risk factors, 13.9% in patients with four risk factors, and 18.6% in those with five or more risk factors, reported Dr. Mishkel, codirector of the coronary catheterization laboratory at St. John's Hospital.

Average hospitalization costs also increased as the number of risk factors accumulated. Patients with no risk factors had an average cost of $9,905. Those with two risk factors had their average costs jump by 26%. Patients with four risk factors had their average costs rise by 70%, and for patients with five or more risk factors the average cost nearly doubled.

A multivariate analysis of the risk factors found that placement of a drug-eluting stent in a previously dilated coronary artery was associated with a 2.3-fold increase in the MACE rate, the greatest impact of any factor on the MACE rate. Other risks linked with jumps in the MACE rate were age of more than 85 years, linked with a 2.1-fold rise in the MACE rate; presence of thrombus, linked with a 77% increase; and multilesion stenting, linked with a 58% rise. Coronary arteries wider than 2.5 mm had a 30% lower MACE rate, compared with narrower vessels. ■

Real-World MACE Rates and Hospital Costs of Drug-Eluting Stents

Risk Factors	Patients (%)	1-Year MACE Rate	Average Hospitalization Costs
0*	20%	6%	$9,905
1	29%	8%	$11,078
2	24%	11%	$12,473
3	16%	14%	$13,942
4	8%	14%	$16,816
≥5	4%	19%	$19,078

*Patients fall within all major trial criteria.
Note: Percentages do not add up to 100 because of rounding.
Source: Dr. Mishkel

DESs Not Always Worth the Price

Routine Use *from page 1*

younger patients with single- or double-vessel disease, short lesions, and large stent sizes fare very well with bare-metal stents."

BASKET involved 826 consecutive patients treated at University Hospital of Basel with angioplasty and stenting for 1,281 de novo coronary lesions. They were randomized to the sirolimus-coated Cypher stent, the paclitaxel-coated Taxus stent, or the cobalt-chromium–based Vision third-generation bare-metal stent (BMS). The study was funded by the university in response to questions from cardiologists and hospital administrators about the impact of the growing use of DESs on the hospital budget.

'It's a difficult task to tell a patient drug-eluting stents are better—as we have shown—but you aren't getting one.'

DR. PFISTERER

Unlike previous randomized stent trials that were funded by device manufacturers and featured highly selected patient populations, BASKET was designed to reflect everyday clinical practice in the catheterization laboratory. Three-fifths of the participants presented with acute MI or unstable coronary syndromes. Sixty-nine percent of enrollees had multivessel disease, and one-half of those had involvement of the left anterior descending coronary artery. Patients received a mean of 1.9 stents with a mean total stent length of 34 mm.

The 6-month combined efficacy end point of cardiac death, MI, or target vessel revascularization occurred in 12.1% of the BMS group and in 7.2% of the DES group. This difference was driven largely by the 43% reduction in target-vessel revascularization in DES-treated patients. There was a consistent trend for fewer major adverse cardiac events with the Cypher, compared with the Taxus DES; however, the sample size was too small to determine statistical significance. The cardiac event rate in the BMS group was lower than might be anticipated in such a relatively high-risk population, most likely because the Vision stent is more effective than the earlier-generation steel stents, the cardiologist observed.

The mean 6-month total costs were 10,544 euros per patient with the DESs and 9,639 euros per patient with the BMS. It cost a mean of 18,311 euros to avoid one major adverse cardiac event through the use of drug-eluting, rather than bare-metal, stents. The estimated cost per quality-adjusted life year gained through the use of drug-eluting in lieu of bare-metal stents was 55,000-73,000 euros, depending on the quality of life measure that was used. Those estimates fall outside the range of what most health economists define as cost-effective therapy.

Kim M. Fox, M.D., professor of clinical cardiology at Royal Brompton Hospital, London, commented that the rapidly growing use of DESs is a huge issue in the United Kingdom, where there is concern that it is a potential hospital budget buster.

He added that although the BASKET trial provides important information about the limitations of the cost-effectiveness of DESs, interventional cardiologists will point to the devices' superior efficacy and find ways to expand their use.

"The interventionists will make all the lesions long and all the vessels small," he quipped.

"Patients will ask for drug-eluting stents more and more," agreed Dr. Pfisterer. "It's a difficult task to tell a patient drug-eluting stents are better—as we have shown—but you aren't getting one."

Discussant Petr Widimsky, M.D., D.Sc., of Charles University, Prague, noted that DESs emerged from BASKET looking a lot better than they would have if investigators had compared them with one of the earlier-generation steel BMSs, which cost roughly half as much as the Vision stent.

"Drug-eluting stents are not saving any costs by reducing the restenosis rate. The opposite is true; the routine use of drug-eluting stents increases health care costs," he said. "Until manufacturers drop the price and make them more affordable for all patients, it's got to be small arteries, large lesions." ■

Revascularization Underused in Cardiogenic Shock

Both percutaneous coronary interventions and coronary artery bypass grafting are seriously underused in patients with MI complicated by cardiogenic shock, according to a nationwide survey.

The American College of Cardiology and the American Heart Association revised their guidelines in 1999, elevating early mechanical intervention for cardiogenic shock to a class I recommendation for patients younger than 75 with an ST-elevation left bundle-branch block acute MI. However, a national database that has tracked practice patterns and MI outcomes since 1990 showed that physicians have been slow to comply with this change and had only marginally increased the use of PCI and CABG in this patient group by early 2004, the most recent year for which data were available, said Anvar Babaev, M.D., of New York University, New York, and colleagues (JAMA 2005;294:448-54).

The database included nearly 300,000 MI patients treated at 775 hospitals with revascularization capability. Of these, more than 25,000 (8.6%) had cardiogenic shock. Mortality clearly decreased with increasing use of revascularization, illustrating the benefit of early mechanical intervention. But physicians may still be reluctant to try these interventions in high-risk patients, the investigators said.

—Mary Ann Moon