EDITORIAL COMMENT

Drug-Eluting Stents for ST-Segment Elevation Myocardial Infarction

Treatment of Choice or Is Discretion the Better Part of Valor?*

Charanjit S. Rihal, MD, MBA, FACC
Rochester, Minnesota

The use of drug-eluting stents (DES) for primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) has generated a variety of responses ranging from enthusiasm to consternation. In this issue of JACC: Cardiovascular Interventions, Shishehbor et al. (1) present observational outcome data on 699 STEMI patients treated with primary PCI at the Cleveland Clinic from 2002 to 2007. The clinical and angiographic characteristics of the cohort are typical of a North American STEMI population, with a mean age about 60 years, majority male, 40% smokers, and about 20% diabetic. Patients were treated with standard regimens of aspirin, clopidogrel, unfractionated heparin, and glycoprotein IIb/IIIa inhibitors. Pre-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 was present in 31%, and post-procedural TIMI flow grade 3 was achieved in 96% of cases overall. Two types of multivariable adjustment were used to address the inherent limitations of the nonrandomized design: Cox multivariable proportional hazards adjustment and propensity analysis of a matched subset of 480 patients. Both analyses indicated that mortality and target lesion revascularization (TLR) were less frequent in patients treated with DES, almost entirely because of a reduction in TLR. Information regarding recurrent nonfatal myocardial infarction is not available, nor is the incidence of stent thrombosis. While encouraging, without these safety data it would be premature to conclude that DES are preferred for STEMI.

This important article raises a number of questions regarding the safety and efficacy of DES usage for primary PCI.

Goals of Primary PCI

Simplistically, the goal of primary PCI is to achieve rapid and complete myocardial reperfusion, which in turn leads to optimal patient outcomes. Both the technical aspects of the PCI itself as well as efficient organization and delivery of PCI must be optimal. In the Shishehbour series, median door-to-balloon time was 109 min, with an interquartile range of 40 to 278 min; clearly there is room for improvement even in expert institutions such as the Cleveland Clinic. Although balloon angioplasty can establish TIMI flow grade 3, bare-metal stents (BMS) reduce the risk of reocclusion or reinfarction after primary PCI. In addition, DES promise improved late angiographic and clinical outcomes. Concerns over late stent thrombosis put a significant damper on enthusiasm for DES in the U.S. in 2007 and raised cautionary flags regarding the use of these complex medical devices in STEMI patients.

Because neither randomized nor registry data suggest a reduction in death or myocardial infarction for DES in comparison with BMS, it begs the question whether restenosis is a worthy consideration at the time of primary PCI. Data from the Cleveland and Mayo Clinics would suggest that it indeed is because a significant minority of patients with restenosis present with acute coronary syndromes (ACS) including recurrent myocardial infarction and most require hospitalization for repeat procedures with their inherent cost, morbidity, and mortality (2,3).

Randomized and Registry Stent Comparisons in Primary PCI

A meta-analysis of 8 randomized trials involving 2,786 patients compared DES and BMS in STEMI patients with 1 to 2 years of follow-up (4). Drug-eluting stents significantly reduced the risk of reintervention (hazard ratio [HR] 0.38, 95% confidence interval [CI] 0.29 to 0.50, p < 0.001). The overall incidence of stent thrombosis (HR 0.80, 95% CI 0.46 to 1.39, p = 0.43), death (HR 0.76, 95% CI 0.53 to 1.10, p = 0.14), and recurrent myocardial infarction (HR 0.72, 95% CI 0.48 to 1.08, p = 0.11) was not significantly different for patients receiving DES versus BMS (4).

These data strongly support the safety and efficacy of DES in STEMI. Despite their advantages for efficacy comparisons, randomized controlled trials have inherent limitations of generalizability because of strict inclusion and exclusion criteria, and the fact patients must be eligible for both treatments. Registry data, on the other hand, usually encompass a much greater variety of patients and can document outcomes of all comers. In this regard, data from...
the Thoraxcenter showed less TLR with DES but at a cost of more stent thromboses. The TLR benefit eroded with time, and after 3 years of follow-up was no longer significant (5).

A so-called real world registry can also reveal the influence of real world biases and perception in influencing stent choice. This trend may be evident in the Cleveland Clinic article, in which utilization of DES for primary PCI rocketed to about 75% of cases after commercial availability in March 2003, and then plummeted to only 15% in 2007, a dramatic turnaround. The reasons for this rapid shift from extreme enthusiasm to extreme caution are unclear, but serve to remind us of the myriad of factors that influence clinical practice.

Theoretic and Practical Issues With DES in STEMI

Even if one accepts that DES are both safe and effective for primary PCI, the task of the interventional cardiologists is not simple. Patient education and informed consent, particularly with regard to subtle and important issues such as late thrombosis, can be challenging in the best of circumstances. In the acute setting, with the JCAHO, CMS, and hospital quality committees scorecarding of our every move and monitoring door to balloon times, it can be extremely difficult to assess the potential for compliance with expensive and prolonged antiplatelet regimens. It can be impossible if the patient is sedated, in shock, or intubated. In such circumstances, late TLR falls off as a consideration and the interventionalist should focus on achieving reperfusion with as few complicating factors as possible. If there is any doubt about the ability of the patient to comply with the usual medical regimens, then discretion may be the better part of valor during an acute procedure.

Thrombus is a near-universal finding in STEMI, and may lead to an unpredictable therapeutic effect when a DES is used. Thrombus trapped between the artery and abluminal surface of the stent can reduce uptake up to 10-fold, whereas clot overlying the stent can shield the drug from washout, thereby increasing uptake into the vessel wall (6). Whether such interactions will influence arterial healing such that clinically important differences in cardiac events will emerge remains to be seen.

To summarize, currently available randomized and observational data point to the safety and efficacy of DES in STEMI but with several caveats and points of emphasis. First, DES do not lower acute or long-term mortality in comparison with BMS. Second, in most patients DES will lead to superior long-term clinical and angiographic results. Third, if an operator uses a BMS for STEMI, this should not be regarded as a failure, particularly if compliance and comorbidity are difficult to assess. Two further pieces of information are needed to clinch the role of DES in STEMI: long-term safety data based on large numbers of patients and large prospective randomized controlled trials.

Current and Future Directions

Although balloon occlusion devices were not proven beneficial when used routinely, early results suggest that mechanical thrombus removal is a useful adjunct before stent deployment (7,8). The HORIZONS (Harmonizing Outcomes With Revascularizations and Stents in Acute Myocardial Infarction) trial is a 3,600-patient prospective randomized controlled trial of STEMI patients comparing primary PCI with a paclitaxel-eluting stent or BMS. Results of the stent comparison arm are due later in 2008. This trial will provide important new information in the field but is unlikely to be the final word because only 1 type of DES is being tested.

Long-term outcomes of DES are contingent on patient compliance with expensive long-term oral antiplatelet drugs, and discontinuation (premature or otherwise) of clopidogrel may be especially hazardous after a STEMI. Resistance to oral antiplatelet drugs is associated with an increased risk of recurrent events after STEMI (9), and although several platelet reactivity assays exist, none are in widespread use at the present time. Point-of-care assays validated with clinical outcomes are needed to identify patients at high risk of recurrent events and to tailor therapy.

As the next generation of DES becomes available in the U.S., these stents will undoubtedly be used in many patients with STEMI, but these stents have not been tested in prospective STEMI trials. Post-market surveillance will be necessary to ensure long-term safety and efficacy for each stent. Perhaps what is needed to advance the field of STEMI intervention further is development of the disease-specific stent technology. Currently, the same DES are used for chronic stable angina as are for ACS, STEMI, or ischemic cardiomyopathy with ventricular arrhythmias. Because the pathobiology of STEMI is inherently different and much more complex than stable angina, it makes intuitive sense that different stents are needed (10). Indeed, an abciximab-coated stent has been developed and tested extensively in Asia (11). Idealistically, specific DES for STEMI that promote plaque healing and rapid endothelization, offer local antiplatelet actions, and modulate left ventricular remodeling are needed. Perhaps that day will not be far into the future.

Reprint requests and correspondence: Dr. Charanjit S. Rihal, Director, Cardiac Catheterization Laboratory, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905. E-mail: rihal@mayo.edu.

REFERENCES


