Drug-Eluting Stents

More Dollars Than Sense?*

Sunil Garg, MD,†‡ Mark J. Eisenberg, MD, MPH‡§
Montreal, Quebec, Canada

The clinical and economic analysis by Eisenstein et al. (1) in this issue of JACC: Cardiovascular Interventions is a welcome addition to the collective literature on the cost-effectiveness of drug-eluting stents (DES). There are limited trial data regarding this topic, and most appraisals have been based on registry assessments. Eisenstein et al. (1) present the long-term clinical and economic analysis of a trial comparing a DES (zotarolimus, Endeavor, Medtronic CardioVascular, Santa Rosa, California) versus a bare-metal stent (BMS) (Driver, Medtronic CardioVascular). The inclusion of data up to 4 years post-index procedure is particularly important given concerns with late stent thrombosis with DES.

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The ENDEAVOR II trial was an international, randomized, double-blind study that assessed the safety and efficacy of the Endeavor DES (2). A total of 1,197 patients with a single, de novo lesion in a native coronary artery were randomized to receive either the Endeavor (n = 598) or Driver (n = 599) stent. The patients had either clinical evidence of ischemia or a positive functional study and could not have had a myocardial infarction in the preceding 72 h. The investigators performed an economic assessment of the patients in the ENDEAVOR II trial with Medicare cost weights and quality-of-life adjustments applied from secondary sources. They compared the differences through a 4-year follow-up period. They found that the Endeavor stent significantly reduced the rate of 4-year target vessel revascularization (TVR) versus the Driver stent. There was no difference in the rates of death or nonfatal myocardial infarction. These findings are consistent with previous DES safety studies for Cypher (Cordis, Johnson & Johnson, Bridgewater, New Jersey) and Taxus (Boston Scientific, Natick, Massachusetts) stents (3,4).

The primary clinical and economic benefit of a DES is the reduction in follow-up TVR and its associated costs. A disease-specific cost-effectiveness analysis was performed to assess the incremental costs per TVR avoided. There was an 11.1% reduction in TVR. Although the index procedure was more expensive in the DES group, the lower rates of follow-up TVR resulted in DES becoming cost neutral. The 4-year cost of a DES approach was $21,873 versus $22,167 for the BMS group.

Prior to the present study, there were 2 other trials that prospectively examined the cost effectiveness of DES compared with BMS in the U.S. The first was conducted as a substudy of the SIRIUS (Sirolimus-Eluting Balloon expandable Stent in the treatment of Patients with De Novo Native Coronary Artery Lesions) trial (3), which compared sirolimus-eluting stents with BMS. The second trial was a substudy of the TAXUS IV trial, which compared paclitaxel-eluting stents with BMS (4).

In the SIRIUS trial, patients randomized to DES had costs of index hospitalization that were higher than patients randomized to BMS. However, patients randomized to BMS had total follow-up costs that were higher than patients randomized to DES. This led to similar cumulative 1-year follow-up costs between the 2 groups. The TAXUS IV trial substudy had similar results. Both trials followed patients for only 1 year. A recently published cost-effectiveness assessment (5) extrapolated data from these trials and included the cost of clopidogrel over an additional 2-year period. After including the extra cost of clopidogrel to prevent late stent thrombosis, the analysis demonstrated a substantially increased cost for DES. The authors concluded that an across-the-board use of DES is not cost-effective in the U.S. in terms of cost per quality-adjusted life year (QALY) gained and cost per TVR avoided.

Eisenstein et al. (1) examined their data and noted that there were no major differences in the utilization of dual antiplatelet therapy between the 2 groups over the 4 years of the study. On the other hand, they were unable to take into account the major shift that has occurred in the management of patients with DES since their data were collected. The trial data were collected between July 2003 and January 2004, and both groups were assigned to 12 weeks of dual antiplatelet therapy. In 2004, the risk of late stent thrombosis had not yet been recognized, and it was considered safe to discontinue dual antiplatelet therapy in patients with Cypher stents at 12 weeks and with Taxus stents at 24 weeks. However, following the discovery of risk of late stent thrombosis for DES, patients are now maintained on dual antiplatelet therapy for a longer period of time.

The investigators demonstrated a statistically insignificant difference between the 2 groups with regards to the use of dual antiplatelet therapy over the 4-year period. However, this does not reflect the current clinical practice of maintaining patients with DES on clopidogrel for a minimum of 1 year, and in

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From the *Division of Cardiology, McGill University Health Centre, and the †Department of Epidemiology, Biostatistics, and Occupational Health and the ‡Divisions of Cardiology and Clinical Epidemiology Jewish General Hospital, McGill University, Montreal, Quebec, Canada.
some cases indefinitely. Prior studies have estimated the costs of such dual antiplatelet therapy to be roughly $2,500 over 2 years (5). If factored over the 4 years of the ENDEAVOR II study, this extra expenditure would increase the cost associated with DES to the point that it would no longer be cost effective. Furthermore, the patients who received BMS could have stopped their dual antiplatelet therapy as early as 4 weeks if no concomitant acute coronary syndrome were present, thus magnifying further the cost differential between the 2 arms.

There are extensive data proving DES effectively reduce the rate of in-stent stenosis and that they are an important tool in the arsenal of interventional cardiologists. Convincing data remain absent, however, that DES are cost saving or that they are cost neutral. A considerable amount of money must be spent for a modest long-term clinical benefit since DES have no impact on mortality or myocardial infarction rates and because their effect on quality of life appears modest (6). Given the ever-increasing scrutiny on health care expenditures and the increasingly important need for fiscal responsibility, an all-embracing use of DES cannot be advocated at this time. DES are likely only to be cost effective in highly selected groups of patients at particularly high risk for restenosis. Given the risk of late stent thrombosis and the need for long-term dual antiplatelet therapy, future studies should include the cost of extended thienopyridine use in order to determine the true cost of DES. In our opinion, a nonselective use of DES currently involves more dollars than sense.

Reprint requests and correspondence: Dr. Mark J. Eisenberg, Divisions of Cardiology and Clinical Epidemiology, Sir Mortimer B. Davis Jewish General Hospital/McGill University, 3755 Cote Ste. Catherine Road, Suite A-118, Montreal, Quebec H3T 1E2, Canada. E-mail: mark.eisenberg@mcgill.ca.

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