Late Thrombosis Haunts Drug-Eluting Stents

Drug-eluting stents now dominate rapid growth of coronary artery stenting because they dramatically cut the rate of restenosis. But a new issue has emerged: late thrombosis. Using data collected to better define the late-thrombosis risk, concern about this complication will haunt drug-eluting stents and dampen their use.

Late thrombosis occurs when a thrombus forms within a stent and abruptly closes the coronary artery a month or more after the stent was placed, a time when bare metal stents are generally believed to have become a benign part of a patient’s vasculature.

‘Late thrombosis has been extremely rare with bare-metal stents,’ noted Mark J. Eisenberg, M.D., an interventional cardiologist at McGill University in Montreal. That’s why a report of four cases of fatal, late thrombosis in patients with drug-eluting stents in The Lancet last October caught cardiologists’ attention. Even more compelling were the circumstances that tied the four cases together. In every patient, the abrupt occlusions appeared about a year after the stents were placed, and soon after the patients stopped long-term aspirin therapy (Lancet 2004;364:1519-21).

A team of physicians from the Thorax Center in Leiden, Netherlands, and from the Washington Hospital Center published the clinical details of four patients who developed stent thrombosis 11-14 months after receiving a drug-eluting stent. Three patients had anterior myocardial infarctions, while the fourth manifested chest pain. Two patients had cardiac infarctions, while the fourth manifested chest pain. Two patients had coronary interventions (SIRIUS) trial, which compared sirolimus-eluting stents with bare-metal stents in a total of 5,103 patients (Lancet 2004;364:1519-21). The results showed that the pooled rate of stent thrombosis was 0.5% among the patients who received bare-metal stents and 0.7% among those who received drug-eluting stents, a non-significant difference. But because the rate of thrombosis is low, even this large analysis did not have the statistical power to completely rule out a twofold difference in risk between the two stent types.

Some additional analyses followed that further combed through the data from trials that had compared drug-eluting and bare-metal stents, and perhaps use a meta-analysis to better define the risk, identify clinical factors that boost a patient’s risk, and determine the optimal duration of antiplatelet therapy.

Develop new strategies to deal with potential interruptions of antiplatelet therapy, including continuing antiplatelet therapy during surgery, and delaying surgery for more than a year after a patient receives a drug-eluting stent.

Drug-Eluting Stents Meet Cost-Effectiveness Standards

By Mitchell L. Zoler
Philadelphia Bureau

Each drug-eluting coronary stent costs a hospital an average of $2,500, about twice the cost of a similar bare-metal stent. Although it looks like the price of drug-eluting stents won’t change substantially for at least another year, even at current prices they save costs for certain high-risk patients and are cost-effective for most. But concerns from patients undergoing percutaneous coronary interventions, said David J. Cohen, M.D., associate director of interventional cardiology at Beth Israel Deaconess Medical Center in Boston.

Two brands of drug-eluting stents, Cypher and Taxus, currently compete in the U.S. market, and even though most experts say that there is little clinically or technically to favor one over the other, their competition is not likely to lead to a substantial price drop anytime soon. "Both companies are selling lots of stents, so they may be happy to keep their current market shares," Dr. Cohen said in an interview. The major shakeup in the market will not come until early next year, when a new wave of patients undergoing percutaneous coronary interventions, said David J. Cohen, M.D., associate director of interventional cardiology at Beth Israel Deaconess Medical Center in Boston.

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"The company of reference is based on the same properties that let drug-eluting stents block restenosis. As explained by Dr. Eisenberg in a comment that accompanied the four case reports, bare-metal stents become endothelialized within a few weeks of implantation, which is why their rate of late thrombosis is so low. In contrast, drug-eluting stents delay endotelization, which is why dual platelet inhibition is routinely used for up to 6 months.

‘I’ve changed the way I use drug-eluting stents’ because of the reports of late thrombosis, said Deepak L. Bhatt, M.D., an interventional cardiologist at the Cleveland Clinic. ‘If I know a patient will have surgery soon, I change my self or he really needs the coronary stent before surgery. I try to defer stenting when possible. If stenting must be done immediately, then I tend to use bare-metal stents. I think most of my colleagues would too,’ Dr. Bhatt said in an interview. The Lancet report found that some cardiologists have taken steps to put even greater emphasis on anti-thrombotic treatment, without cutting back on using drug-eluting stents. ‘The reports of subacute stent thrombosis have not prompted me nor any other interventional cardiologist who I know to change practice, other than to extend the duration of dual oral antiplatelet therapy,’ said Herbert D. Aronow, M.D., director of the cardiac catheterization laboratories at the Veterans Affairs Medical Center in Philadelphia. ‘I typically continue aspirin and clopidogrel through surgery, if possible. When not possible, I try to continue aspirin alone. If both aspirin and clopidogrel must be stopped, I typically delay surgery until the risk of stent thrombosis is much lower, and I balance the need for surgery against the risk of stent thrombosis.

‘If we find that the late thrombosis rate is two- or threefold higher [with drug-eluting stents, compared with bare-metal stents], I would prefer dual antiplatelet therapy for a year after an implant, then we will need to reconsider our use patterns of drug-eluting stents until we develop safer systems,” Martin B. Leon, M.D., said at the American Heart Association scientific sessions last November in New Orleans. ‘Safety is more important in this case than anti-estrogenic efficacy,’ added Dr. Leon, associate director of the Center for Interventional Vascular Therapy at Columbia University in New York. From the time drug-eluting stents were introduced, physicians were concerned about an increased incidence of late thrombosis. Last year, Dr. Eisenberg and his associates did a meta-analysis of data collected in 11 trials that had compared sirolimus- and paclitaxel-eluting stents with bare-metal stents in a total of 5,103 patients (Lancet 2004;364:1519-21). The results showed that the pooled rate of stent thrombosis was 0.5% among the patients who received bare-metal stents and 0.7% among those who received drug-eluting stents, a non-significant difference. But because the rate of thrombosis is low, even this large analysis did not have the statistical power to completely rule out a twofold difference in risk between the two stent types.

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This means that drug-eluting stents are cost-effective for the majority of patients who get them, Dr. Cohen said during a talk at the American Heart Association’s scientific sessions last November in New Orleans. Dr. Cohen and his associates tested these assumptions with data collected from four recent trials. In the Sirolimus-Eluting Stent in De Novo Native Coronary Lesions (SIRIUS) trial, which compared sirolimus-eluting stents (Cypher) with bare-metal stents, the 1-year incremental cost of the drug-eluting stent was $309 per patient. The cost per repeat revascularization avoided was $27,000. In the TAXUS IV trial, paclitaxel-eluting stents (Taxus) were compared with bare-metal stents. The cost-effectiveness rates were $760 for each repeat revascularization avoided and $5,105 for each quality-life year gained.

However, the study did not routinely specify antiplatelet therapy, and instead relied on clinical assessment of patients undergoing percutaneous coronary interventions. Dr. Cohen has received research grants from Cordis, which markets the Cypher stent, and from Boston Scientific, which markets the Taxus stent.