The Risk of Stent Thrombosis after Coronary Arterial Stent Implantation

One of the most dreaded complications after percutaneous coronary arterial angioplasty is stent thrombosis. This serious untoward event usually results in acute myocardial infarction with high mortality. Stent thrombosis often occurs early, within 30 days of implantation, in patients who receive bare metal coronary arterial stents. However, patients undergoing drug-eluting stent implantation infrequently develop late stent thrombosis many months and even years after the deployment of these devices. Fortunately, stent thrombosis is a rather uncommon event.

Factors that favor stent thrombosis include technical problems during stent implantation; patients who undergo stent placement after an acute coronary syndrome or when diabetes mellitus is present; and patients with an intrinsic resistance to antiplatelet therapy. The most important factor leading to stent thrombosis is discontinuation of antiplatelet therapy, particularly clopidogrel administration. Because late stent thrombosis is mainly a complication of drug-eluting stent deployment, prolonged clopidogrel and aspirin therapy is essential for such individuals. As already noted, bare metal stent thrombosis usually occurs during the first 30 days after stent implantation, and thus, clopidogrel therapy may be discontinued after at least 1 month of administration in these patients. However, many cardiologists favor 3 months of continuous clopidogrel therapy after bare metal stent placement. Healing of the endothelium over drug-eluting stents has been shown to be impaired secondary to antimitabolites impregnated in the stent coating. Incomplete endothelial healing has been documented occasionally in patients who received a drug-eluting stent more than 2 years earlier. It is believed that incomplete endothelial covering of stent struts is the cause of incipient stent thrombosis. Consequently, aspirin and clopidogrel therapy should be continued for at least 12 months after drug-eluting stent placement. At this time, it is still unclear whether dual antiplatelet therapy can be discontinued after as little as 12 months of continuous administration in patients with drug-eluting stents. Ongoing studies are addressing this issue, and clinicians should watch for published results of such studies in the near future. In our own practices, if patients tolerate dual antiplatelet therapy and can afford the expense of clopidogrel, we usually continue dual therapy for at least 2 years and sometimes indefinitely in patients with evidence of atherosclerotic arterial disease in other regions, for example, carotid or femoral arteries.

Difficulties arise for cardiologists and other clinicians caring for patients with drug-eluting stents under 3 circumstances. First, poor patient compliance because of personal factors or clopidogrel expense; the problem of expense is often a difficult one to address. Clinicians should understand the patient’s financial situation before stent implantation. If clopidogrel therapy will represent a financial hardship for the patient, a bare metal stent should probably be used. The second problem involves bleeding complications secondary to or enhanced by dual antiplatelet therapy. The final issue involves patients who require urgent or elective surgery and who are taking aspirin and clopidogrel.

The first problem should be dealt with before stent implantation when informed consent is obtained for the percutaneous coronary intervention procedure. As already noted, patients who are deemed high risk for poor compliance should be carefully counseled concerning the need for continuous antiplatelet therapy after stent placement and its associated cost. If the clinicians involved in the care of such patients continue to be concerned about compliance, a bare metal stent should probably be used rather than a drug-eluting device.

The second difficulty, bleeding complications, can be addressed by controlling the source of bleeding and, at times with great care, by modestly reducing the dosages of aspirin and clopidogrel. A particularly high-risk situation for potential bleeding complications occurs in patients who are taking warfarin for stroke prophylaxis, for example, secondary to atrial fibrillation, and who then undergo percutaneous coronary intervention with deployment of a drug-eluting stent. These patients are now placed on triple anticoagulant therapy (aspirin, clopidogrel, and warfarin), and they are at very high risk for bleeding. A number of cardiologists try to keep the international normalized ratio close to 2.0 in such patients in an attempt to prevent hemorrhage. Whether this strategy truly results in less bleeding is not known at this time. However, this approach would seem to be rational.
Another issue for patients who undergo coronary stent insertion involves the need for elective or urgent surgery after drug-eluting stent deployment. Antiplatelet therapy in this setting, and especially clopidogrel therapy, is associated with increased postoperative bleeding. Bleeding complications can be catastrophic if a neurosurgical intervention is planned. In other surgical situations, bleeding may lead to transfusions with attendant potential complications. Many, but not all, surgeons are unhappy about operating on patients who have recently undergone drug-eluting stent implantation and who require continuous aspirin and clopidogrel therapy. If the planned surgical intervention is elective, it is often prudent to delay the operation until the patient with a drug-eluting stent has been on dual antiplatelet therapy for at least 1 year. If the surgery is urgent, postoperative therapy with an intravenous IIb/IIIa glycoprotein blocker for several days followed by resumption of dual oral antiplatelet therapy is one possible option. A second option involves the administration of full therapeutic doses of heparin with discontinuation of antiplatelet therapy for as short a time period as possible during the perioperative period. There are insufficient data available at this time to assist cardiologists and clinicians in deciding which of these 2 strategic options to select. Consultation with surgical colleagues and perhaps a hematologist may assist in the decision-making process. If surgery is urgent but not an emergency, patients can discontinue clopidogrel and aspirin therapy for 5 to 7 days before the planned surgical intervention and receive “bridging therapy” with heparin, as mentioned above. Heparin therapy is discontinued on the morning of surgery, resumed during the early postoperative period, and continued for several days thereafter until dual antiplatelet therapy has been resumed, often with a loading dose of 300 to 600 mg of clopidogrel. Minor surgery, such as dental, dermatologic, or cataract surgery, can almost always be performed without discontinuing dual antiplatelet therapy. Internists clearly need to work closely with surgical and cardiology colleagues when such patients are sent for surgical intervention.

One final issue that has been discussed recently in the medical literature involves attenuation of the antiplatelet action of clopidogrel by proton pump inhibitors. The proton pump inhibitor omeprazole inhibits one of the isoenzymes in the CYP2 receptor family, thereby diminishing the antiplatelet activity of clopidogrel. The clinical significance of this drug–drug interaction is uncertain. The Food and Drug Administration has issued a warning concerning this interaction, but clinical studies are mixed as to its effect. Currently, there is no conclusive answer; however, some experts recommend continuing proton pump inhibitor therapy if indicated by a documented risk for gastrointestinal bleeding. Some clinicians favor switching from omeprazole to another proton pump inhibitor or to a histamine H2 receptor blocker, but this has not been conclusively proven to be an efficacious strategy. Concomitant use of clopidogrel and a proton pump inhibitor in patients with an acute coronary syndrome was associated with an increased risk of adverse outcomes compared with the use of clopidogrel without a proton pump inhibitor. This finding suggests that the concomitant use of a proton pump inhibitor may be associated with attenuation of the benefits of clopidogrel after an acute coronary syndrome.

Stent thrombosis is a potentially life-threatening complication after coronary stent implantation. Every effort should be made to convince patients to continue dual antiplatelet therapy for at least 30 days after bare metal stent deployment and for 12 months after drug-eluting stent placement. Patients who require surgery after stent implantation currently represent a challenge for the clinicians involved in their care.

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References