Coronary Stent Occlusion: Thrombus Horribilis*

JOHN A. BITTL, MD, FACC
Boston, Massachusetts

Coronary stenting has revolutionized the practice of interventional cardiology. Coronary stenting has rapidly evolved and supplanted other interventional approaches because of its excellent angiographic results and low rates of clinical and angiographic restenosis. When two randomized trials (1,2) showed that stenting could reduce restenosis by 30% compared with balloon angioplasty in patients with primary lesions in large native coronary arteries, it was anticipated that stents would be used for this indication in ~10% of patients undergoing angioplasty. After several studies showed that coronary stenting could be used to treat abrupt vessel closure during balloon angioplasty (3), stenting was rapidly incorporated in interventional cardiology to reduce the need for emergency bypass surgery.

Coronary stenting, however, has not been restricted to the prevention of native-vessel restenosis or the treatment of abrupt vessel closure. Coronary stenting is widely used to treat complex lesions previously deemed to be too high risk for conventional balloon angioplasty (4,5), as "off-label" treatment for complex or saphenous vein graft lesions (6) not formally approved by the Food and Drug Administration and as a means to treat minor dissections or residual stenoses during conventional angioplasty that were previously regarded as borderline but now judged to be suboptimal by current standards. It is estimated that >300,000 of the 884,000 interventional procedures performed worldwide during 1995 involved the use of coronary stents (7).

Subacute thrombosis. Unfortunately, coronary stenting is associated with a unique and sobering complication, Sudden and complete occlusion of the stent occurs in ~4% of patients within 2 days to 4 weeks after implantation (8,9). Occlusion of stents differs strikingly in timing and severity from abrupt vessel closure after conventional balloon angioplasty. Complete vessel closure after angioplasty also occurs in ~4% of patients but peaks in incidence while the patient is still in the cardiac catheterization laboratory, where the problem can be recognized and treated, and causes major ischemic complica-

*Editorials published in the Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

Address for correspondence: Dr. John A. Bittl, Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Boston, Massachusetts 02115.
emphasized the need to post-dilate stents with high pressure balloons to achieve complete stent expansion. This strategy was initially revealed and substantiated by intravascular ultrasound (IVUS) imaging, which frequently showed inadequate stent expansion when conventional balloon techniques were used for deployment. Now that high pressure balloon inflations are routinely used, a polite debate has arisen regarding the need for IVUS imaging. Currently, some investigators can visualize suboptimal results with IVUS imaging in almost 50% of patients undergoing coronary stenting guided by angiography (18-20), whereas others point to a lack of proven clinical benefit from IVUS imaging over angiography (21-23).

Several advances in antithrombotic therapy have also reduced the risk of stent thrombosis. Although warfarin anticoagulation was used in patients treated with stents in the patients from the Mayo Clinic (8) and in randomized studies (1,2) based on the best information available at the time, it may not be the optimal antithrombotic therapy to prevent stent thrombosis. Recently, Neumann et al. (11) reported that activation of platelet fibrinogen receptors, not an elevation in plasma fibrinogen or other markers of coagulation, increased the risk of stent thrombosis. Schömig et al. (24) observed that the antiplatelet agent ticlopidine resulted in a lower rate of stent thrombosis than anticoagulant therapy in a randomized study involving 517 patients (5.4% vs. 0.8%, p = 0.004). In a pooled analysis of 2,630 patients treated without anticoagulation in whom IVUS imaging was rarely used to guide stent deployment, Mak et al. (9) reported that only 33 (1.3%) developed stent thrombosis.

Recommendations for avoiding stent thrombosis include careful attention to stent deployment technique and antithrombotic therapy. Residual filling defects within the stent, representing fragments of extruded atheromatous plaque or small thrombi, should be treated with additional high pressure balloon inflations or placement of a short stent. Marginal dissections at the proximal inflow or distal outflow of the stent should be corrected with additional stents. Patients who receive stents in high risk settings, such as acute myocardial infarction, abrupt closure or preexisting thrombus, should be considered for intensive antithrombotic therapy with prolonged anticoagulation or platelet receptor IIb/IIIa blockers (25). Although ticlopidine is superior to warfarin anticoagulation therapy and platelet IIb/IIIa receptor blockers such as the monoclonal antibody c7E3 are theoretically appealing as a means to prevent stent thrombosis, it must be emphasized that no antithrombotic regimen has been identified to prevent thrombosis of a suboptimally deployed stent. If a technically perfect stent result cannot be obtained, as judged by angiography or IVUS imaging, the ineluctable conclusion is that coronary artery bypass surgery should be considered for all good surgical candidates to prevent the potentially serious complications caused by subacute stent thrombosis.

New stent designs could have a major impact on the risk of stent thrombosis (26). In the Benestent-II Pilot Study involving 207 consecutive patients (27), the use of an investigational heparin-coated stent did not cause documented stent thrombosis in any patient. Although the absence of stent thrombosis may be attributed to the heparin coating of the stent, other factors associated with a low risk of stent thrombosis in this study included the extensive experience of the team involved in placing stents and exclusion of patients with unstable angina, myocardial infarction or abrupt vessel closure. Although these preliminary results provide a glimmer of hope for reducing stent thrombosis, it is difficult to judge whether the results are generalizable to the worldwide interventional community implanting stents for a broader range of indications, each of which carries a finite risk for stent thrombosis.

**Treatment of stent thrombosis.** If stent thrombosis occurs despite all efforts to prevent it, the initial treatment should follow the approach of Hasdai et al. (8) using immediate repeat angioplasty and bypass surgery if needed. It seems intuitive, however, that repeat use of the same balloon inflation strategy that led to the first episode of stent thrombosis falls short of a more definitive strategy required to prevent a second episode. In contrast, repeat inflation with a larger balloon or a noncompliant balloon to a higher pressure may reduce the risk of recurrent stent thrombosis if the initial episode of stent thrombosis can be attributed to underexpansion of the stent. If adjunctive antithrombotic therapy is required, the theoretical disaggregating action of platelet IIb/IIIa receptor blockers makes these agents more appealing than fibrinolytic agents. If no correctable cause of stent thrombosis can be identified, bypass surgery is indicated. Bypass surgery was used in 9 of 29 patients with stent thrombosis at the Mayo Clinic (8).

**Conclusions.** Coronary stenting is evolving rapidly. Evidence-based guidelines for coronary stenting will also change rapidly. In the meantime, careful case and vessel selection, optimal stent deployment and improved antithrombotic therapy are steps toward reducing the incidence of stent occlusion. Better studies are urgently needed to define the risk factors and optimal treatment for stent thrombosis. In the long term, a better understanding of the biology of coronary stents from experimental and clinical studies is needed to eliminate the serious problem of stent thrombosis.

**References**