Coronary Angioplasty and Intracoronary Thrombolysis Are of Limited Efficacy in Resolving Early Intracoronary Stent Thrombosis

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Objectives. This study sought to evaluate treatment of early intracoronary stent thrombosis.

Background. Although refinements in intracoronary stent implantation technique and pharmacologic treatment have reduced the frequency of early stent thrombosis, stent thrombosis remains a feared complication of this procedure. Optimal treatment for stent thrombosis is still undefined.

Methods. Twenty-nine patients (44 stents) with early (<30 days) coronary stent thrombosis over a 5-year period at our institution were identified. Treatment and outcome of stent thrombosis were analyzed.

Results. Mean (±SD) time from implantation to stent thrombosis was 6.1 ± 5 days. Twenty-three patients were treated with catheter-based therapies (angioplasty alone in 14, angioplasty and intracoronary urokinase in 7, intracoronary urokinase alone in 2). Flow was restored without residual thrombus in 11 (48%) of the catheter-treated patients (6 of 14 with angioplasty alone, 4 of 7 with angioplasty and urokinase, 1 with urokinase alone). Of the 23 patients, 2 died despite restoration of anterograde flow, and 9 were referred for emergent or urgent bypass surgery because of residual thrombus and refractory angina despite restoration of blood flow. Of the remaining six patients, five were treated medically and one with coronary bypass surgery; three died. Acute myocardial infarction evolved in 26 patients (90%), including 20 (87%) of the 23 catheter-treated patients.

Conclusions. Stent thrombosis is associated with severe adverse outcomes. Although catheter-based therapies are effective in restoring patency in a majority of patients, patients are referred frequently for coronary bypass surgery because of residual thrombus and refractory angina. These findings suggest that alternative or adjunctive therapies for stent thrombosis are needed.

(J Am Coll Cardiol 1996;28:361-7)

Intracoronary stents have become an important addition to the current practice of angioplasty. The most feared complication related to stent placement is early stent thrombosis, which has occurred in the past with a frequency of up to 12% (1-5). As a result of recent refinements in stent implantation technique and postprocedural pharmacologic treatment, the incidence of stent thrombosis after implantation of coronary stents is reported to be lower (6) than the rate of 3.5% reported in the two initial randomized studies comparing coronary angioplasty and stent placement in elective de novo lesions (7,8). Although previous studies have characterized the patients at risk for stent thrombosis (1-5), there are few data pertaining to the optimal therapeutic approach to stent thrombosis. Catheter-based therapies for stent thrombosis are applied frequently in clinical practice (2,3,5,9), yet their efficacy has not been evaluated in a large group of patients. We thus examined the therapeutic approaches and clinical course of all patients with early stent thrombosis at our institution over a 5-year period.

Methods

Study protocol. The study protocol was approved by the Mayo Clinic Institutional Review Board. We performed a retrospective analysis of the Mayo Clinic coronary intervention data base, obtaining data pertaining to all patients who had stents placed with a follow-up period of at least 6 months after the procedure. Of all patients who had intracoronary stents placed between January 1990 and June 1995, we scrutinized the records of those who had repeat angiography, intervention, coronary bypass surgery, acute myocardial infarction or death within 30 days of stent implantation. Early stent thrombosis was defined clinically as the sudden onset of chest pain associated with electrocardiographic (ECG) changes in the distribution of the target vessel suggestive of acute ischemia or infarction, occurring within 30 days of stent placement. In patients in whom coronary angiography was performed, stent thrombosis was confirmed if there was occlusion (Thrombolysis in Myocardial Infarction [TIMI] flow grade 0 or 1) within the stent with angiographic evidence consistent with thrombus (discrete occlusive intraluminal filling defect of convex curvature within or adjacent to the stenotic region [2,10]).

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diagnosis of thrombus was made if there was one or more lumen filling defects in the absence of a major dissection (10). Probable diagnosis of thrombus was made if there were lumen filling defects with minor dissection (linear extraluminal cap in orthogonal views without lumen compromise) (10) or if the lumen appeared to be hazy in orthogonal views. Abrupt closure after coronary angioplasty or stent placement may result from coronary artery dissection or formation of intracoronary thrombus, or both (11). In our study, we excluded patients in whom it was believed that the primary mechanism for abrupt closure after stent placement was significant coronary artery dissection remote from the stent site, without definite evidence of thrombus within the stent (10).

Medical records of all patients who had early stent thrombosis after stent implantation were reviewed. The records of patients who were admitted to the hospital for stent thrombosis at outside medical institutions were also obtained and analyzed. Angiographic data acquired during stent placement were reviewed, including target vessel, extent of coronary artery disease (defined as the number of major epicardial arteries with \( \geq 50\% \) diameter stenosis in addition to \( \geq 70\% \) diameter stenosis of the target vessel), percent diameter stenosis before and after stent deployment (visual assessment), TIMI flow grade after stent placement and presence of dissection (filling defect within vessel wall [2,10]) or thrombus during the procedure. Indications for stent deployment were categorized as either elective (for recurrent restenosis or complexity of lesion), treatment of abrupt closure after coronary angioplasty (worsening stenosis with TIMI grade 0 or 1 flow [2,10,11]) or suboptimal angioplasty result (with or without dissection), International normalized ratio (INR) of prothrombin time values for patients receiving warfarin and activated partial thromboplastin time values for patients receiving heparin were documented at the time of stent thrombosis.

For all patients, the therapeutic strategy used for stent thrombosis and the clinical outcome (evolution of myocardial infarction, referral for urgent or emergent coronary artery bypass graft surgery or death) were noted. Acute myocardial infarction was defined when at least two of the following three criteria were met (12): 1) chest pain >30 min, 2) persistent ECG changes, or 3) characteristic elevations in serum creatine kinase (CK) levels with a corresponding increase in MB isoenzyme. In patients treated with catheter-based therapies (angioplasty; angioplasty and intracoronary thrombolysis; or intracoronary thrombolysis alone), percent diameter stenosis before and after the intervention, postprocedural TIMI grade flow and presence of residual thrombus were noted.

Angioplasty technique for stent implantation. All angioplasty procedures were performed using standard techniques (13) through the femoral artery. Intracoronary stent implantation techniques evolved over the study period. Gianturco-Roubin (Cook Inc.) and Wiktor (Medtronic Inc.) stents were generally placed across target lesions using 0.046-cm (0.018-in.) extra support guide wires for delivery, as described previously (14,15). Coronary and biliary Palmaz-Schatz stents (SDS, Johnson & Johnson Interventional Systems) were positioned within the delivery sheath or on the balloon catheter, respectively, over 0.036-cm (0.014-in.) extra support guide wires (followed by retraction of the sheath in the case of coronary stents) (16). Delivery balloons were inflated to nominal pressure. As of 1994, stent delivery has been routinely followed by high pressure (\( \geq 14 \) atm) balloon inflations using noncompliant or minimally compliant balloons at sizes equivalent to or slightly larger than nominal stent size to achieve residual diameter stenosis <20% without intraluminal filling defects. Intravascular ultrasound was used to evaluate stent deployment at the discretion of the operator.

All patients received preprocedural oral aspirin (325 mg) and received intraprocedural heparin to achieve an activated clotting time >300 s. Until 1994, patients received dextran immediately before the procedure in accordance with the stent manufacturer's instructions. Our protocol for stent implantation until late 1994 included warfarin (target INR of 2.0 to 4.0), aspirin (81 to 325 mg once daily) and dipyridamole (75 mg three times daily). As of late 1994, warfarin was administered only to patients with suboptimal stent deployment as assessed by coronary angiography or intravascular ultrasound or with an unfavorable clinical profile. Otherwise, patients were treated indefinitely with aspirin (81 to 325 mg once daily) and ticlopidine (250 mg twice daily) for 4 to 6 weeks.

Angioplasty technique for stent thrombosis. Patients with suspected early stent thrombosis were taken immediately to the catheterization laboratory, and angiography was performed using standard percutaneous techniques through the femoral artery or cutdown of the brachial artery. Once stent thrombosis was confirmed and a decision was made to proceed with angioplasty with or without intracoronary thrombolytic therapy at the discretion of the operator, the occlusion was generally crossed with a soft/floppy guide wire, ensuring that the wire passed freely through the stent lumen. The guide wire was shaped to have an exaggerated “J” or “C” curve at its tip to facilitate passage through the occluded stent. Once the guide wire was passed distally, over-the-wire techniques were used and balloon catheters were advanced and inflated at the occlusion site. Balloon sizes were selected to achieve residual diameter stenosis <20% without intraluminal filling defects. Specific balloon size selection and inflation pressures were at the discretion of the operator. When intracoronary urokinase was administered, the drug was delivered through the guiding catheter or through the angioplasty catheter or drug-infusion catheter.

Statistics. Comparison of patients who subsequently developed early stent thrombosis with those who did not was performed using the Student t-test for continuation variables and the chi-square test for discrete variables; \( p \) values \( \leq 0.05 \) were considered significant.
were younger, had a higher incidence of smoking, had a higher 
who received intracoronary stents but without subsequent 
placement and 10–11% after stent placement. Intraluminal 
rate of previous myocardial infarction and had lower choles-
terol levels. In all, 44 stents had been placed in patients with 
stent deployment

Warfarin. Nine patients had INR values ->2. The remaining 12 
thrombosis were available in 21 of the 25 patients treated with 
procedure (target activated clotting time >300 s), patients 
were maintained on anticoagulant and antithrombotic agents 
as deemed necessary by the attending physician. A detailed 
account of anticoagulant and antithrombotic therapy on pre-

Stent thrombosis. Five of the 29 patients died after stent 
thrombosis, and 26 had an acute myocardial infarction. Treat-

filling defects consistent with thrombus were evident angiog-
raphically before stent placement in 14 (48%) of 29 patients; 
the angiographic diagnosis of thrombus was graded as proba-
ble in 5 patients and as definite in 9. Coronary artery dissection 
was evident angiographically in eight patients (28%); in two 
patients the dissection was external to the stent, and in the 
remaining six patients there were mild to moderate residual 
dissections distal to the segment receiving the stent. High 
pressure balloon inflations were performed during initial stent 
placement in 11 (38%) of 29 patients. Intravascular ultrasound 
or coronary angioscopy was used to evaluate the success of 
stent deployment in four and one patients, respectively; TIMI 
grade 3 flow was evident in all patients at the end of the 
procedure. After receiving intravenous heparin during the 
procedure (target activated clotting time >300 s), patients 
were maintained on anticoagulant and antithrombotic agents 
as deemed necessary by the attending physician. A detailed 
account of anticoagulant and antithrombotic therapy on pre-

Table 1. Demographic, Clinical and Angiographic Profile of Study Patients With Intracoronary Stents With and Without Early Stent Thrombosis

<table>
<thead>
<tr>
<th></th>
<th>Stent Thrombosis (n = 29)</th>
<th>No Stent Thrombosis (n = 732)</th>
<th>p</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>58 ± 14</td>
<td>63 ± 11</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (72%)</td>
<td>540 (74%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>23 (79%)</td>
<td>569 (78%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>23 (79%)</td>
<td>388 (53%)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (17%)</td>
<td>140 (19%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13 (45%)</td>
<td>408 (56%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>9 (31%)</td>
<td>379 (52%)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>11 (38%)</td>
<td>112 (15%)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>14 (48%)</td>
<td>355 (49%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Previous coronary bypass surgery</td>
<td>5 (17%)</td>
<td>241 (33%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Extent of coronary artery disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One vessel</td>
<td>10 (34.5%)</td>
<td>238 (32.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two vessels</td>
<td>9 (31%)</td>
<td>293 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three vessels</td>
<td>10 (34.5%)</td>
<td>201 (27.5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data presented are mean value ± SD or number (%) of patients.

Results

Study cohort. Of 761 consecutive patients in whom intra-
coronary stents had been implanted, 29 with early thrombotic 
occclusion of coronary artery stents were identified (3.8%). 
Follow-up was complete for all patients who received intra-
coronary stents. The demographic and clinical profile of the 
patient cohort is presented in Table 1. Compared with patients 
who received intracoronary stents but without subsequent 
eye stent thrombosis, patients with early stent thrombosis 
were younger, had a higher incidence of smoking, had a higher 
rate of previous myocardial infarction and had lower choles-
terol levels. In all, 44 stents had been placed in patients with 
eye stent thrombosis (one stent in 18, two stents in 3, three 
stents in 2, four stents in 1). Thirty-three Gianturco-Roubin 
stents were placed in 23 patients, seven Palmaz-Schatz stents 
were placed in 5 patients, and four Wiktor stents were placed 
in 2 patients. One patient received one Palmaz-Schatz and one 
Gianturco-Roubin stent. Stent thrombosis occurred 6.1 ± 5 
days (mean ± SD, range 0 to 20) after stent implantation; stent 
thrombosis occurred within 24 h (early) in 4 patients and 
between 1 and 30 days after stent placement (subacute) in 25. 
Angiographic confirmation of stent thrombosis was available 
for 27 patients (93%).

Stent placement and pharmacologic therapy. Indications 
for stent placement are presented in Table 2. Seven patients 
had stents placed for acute myocardial infarction. Table 3 
describes the distribution of treated vessels. One patient had 
stents placed in both the left anterior descending and left 
circumflex coronary arteries. Mean nominal balloon and stent 
sizes were 3.3 ± 0.4 and 3.2 ± 0.4 mm (range 2.5 to 4), 
respectively. Mean vessel diameter stenosis was 54 ± 23% 
after predilation with a balloon catheter and before stent 
placement and 10 ± 11% after stent placement. Intraluminal

Table 2. Indications for Initial Stent Placement for Entire Group and for Subgroup of Patients With Stents Placed in Setting of Acute Myocardial Infarction

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>5</td>
</tr>
<tr>
<td>Abrupt closure after angioplasty</td>
<td>2</td>
</tr>
<tr>
<td>Suboptimal angioplasty</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
</tr>
<tr>
<td>Patients with stents placed in setting of acute myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Abrupt closure after angioplasty</td>
<td>2</td>
</tr>
<tr>
<td>Dissection after angioplasty</td>
<td>1</td>
</tr>
<tr>
<td>Adjunctive therapy for suboptimal direct angioplasty</td>
<td>3</td>
</tr>
<tr>
<td>Rescue angioplasty after failed thrombolytic therapy</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 3. Distribution of Target Vessels in Which Stents Were Placed

<table>
<thead>
<tr>
<th>Target Vessel</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior descending coronary artery</td>
<td>16</td>
</tr>
<tr>
<td>Left circumflex coronary artery</td>
<td>6</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>6</td>
</tr>
<tr>
<td>Saphenous venous bypass graft*</td>
<td>2</td>
</tr>
</tbody>
</table>

*To left anterior descending and right coronary arteries.
Table 4. Anticoagulant and Antithrombotic Therapy in Patients Presenting With Stent Thrombosis

<table>
<thead>
<tr>
<th>Therapy</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin Aspirin Warfarin Ticlopidine Dipyridamole</td>
<td></td>
</tr>
<tr>
<td>+ + + + +</td>
<td>1</td>
</tr>
<tr>
<td>+ + + +</td>
<td>5</td>
</tr>
<tr>
<td>+ + +</td>
<td>8</td>
</tr>
<tr>
<td>+ +</td>
<td>2</td>
</tr>
<tr>
<td>+ +</td>
<td>5</td>
</tr>
<tr>
<td>+ +</td>
<td>4</td>
</tr>
<tr>
<td>+</td>
<td>1</td>
</tr>
<tr>
<td>+ +</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
</tr>
</tbody>
</table>

*See text for specific doses.

Non-catheter-based treatment. Five patients were treated medically (with antianginal therapy but no thrombolytic agents), four because of severe, comorbid underlying disease and one because the area at risk was assessed to be small. Two of these patients died within 17 and 30 days after a protracted and complicated hospital period. One additional patient was sent directly to emergency coronary bypass surgery after coronary angiography had confirmed stent thrombosis and placement of intraaortic balloon pump but died shortly after operation.

Catheter-based therapies. The remaining 23 patients were treated with catheter-based therapies (Fig. 1). Mean vessel diameter stenosis in these patients was improved from 98 ± 7% to 35 ± 34%. Mean nominal balloon size at stent deployment and during treatment for the stent thrombosis was similar (3.3 ± 0.4 mm at stent deployment vs. 3.4 ± 0.4 mm for stent thrombosis). High pressure balloon inflations were performed during angioplasty in one patient for treatment of stent thrombosis, and in two patients after stent deployment during treatment of stent thrombosis. Intracoronary urokinase doses varied. Among five patients treated with angioplasty and urokinase, a bolus of 250,000 U (three patients) or 500,000 U (two patients) was delivered over 10 to 20 min. Two additional patients received prolonged intracoronary infusions of urokinase (for ~12 h) at a rate of 100,000 U/h (after a bolus of 250,000 U in one patient). Both patients who were treated with intracoronary urokinase alone (i.e., without angioplasty) received a total of 250,000 U over 10 to 20 min.

In 11 (48%) of 23 patients, TIMI grade 3 flow was achieved without evidence of residual stent thrombosis (6 of 14 with angioplasty alone, 4 of 7 with angioplasty combined with intracoronary urokinase, 1 with intracoronary urokinase alone). Anterograde flow could not be restored in two patients treated with angioplasty alone; one was managed medically, and the other was referred immediately for emergency coronary bypass surgery. Nine (43%) of 21 patients treated with angioplasty (3 with adjunctive intracoronary urokinase infusion) were referred for emergent or urgent coronary bypass surgery (mean 2 ± 3.9 days, median 1) because of the presence of residual thrombus and continuing angina despite restoration of normal anterograde blood flow. Four of these nine patients were sent immediately from the catheterization laboratory to bypass surgery, three were sent within 24 h, and the remaining two patients 3 and 12 days after angioplasty (six patients had lesions in the left anterior descending coronary artery, two in the left circumflex coronary artery and one in the right coronary artery). Additional stents (one Palmaz-Schatz and one Gianturco-Roubin) were placed in two patients treated with angioplasty and intracoronary urokinase; one was referred for emergent coronary bypass surgery because of residual thrombus.
thrombus, and the other recovered uneventfully. Acute myocardial infarction evolved in 20 (87%) of the 23 patients treated with catheter-based therapies, with a mean peak serum CK value of 1,928 ± 1,610 U/liter.

Two patients died 11 and 15 days after catheter-based treatment of stent thrombosis, although TIMI grade 3 anterograde flow had been restored. One of these had received intracoronary urokinase infusion alone (bolus of 250,000 U), and another had been treated with angioplasty and intracoronary urokinase infusion (bolus of 250,000 U followed by infusion of 100,000 U/h for 12 h). Autopsy in the latter patient revealed acute platelet-fibrin thrombotic occlusion of stent sites with platelet-fibrin emboli within small intramural coronary arteries, resulting in spotty transmural acute myocardial infarction (Fig. 2).

Discussion

The results of our study are in accord with previous data demonstrating that early stent thrombosis is associated with a poor clinical outcome; 26 of 29 patients had an acute myocardial infarction, and 5 died. Moreover, catheter-based therapies for stent thrombosis were found to be only modestly effective in the treatment of early stent thrombosis. Although TIMI grade 3 flow was restored in 21 of 23 patients treated with catheter-based therapies, 20 of these patients developed an acute myocardial infarction (87%), and 9 were referred for urgent or emergent coronary bypass surgery because of residual thrombus threatening reclosure of the treated vessel. Of the 11 patients who underwent coronary bypass surgery (of whom 10 were treated with prior catheter-based therapies), 1 died.

Previous studies. Most available data regarding management of early stent thrombosis are derived from reports describing experience with a single stent design and from relatively small numbers of patients. Nath et al. (2) reported that among 145 patients who underwent Gianturco-Roubin stent placement for abrupt vessel closure or for prevention of restenosis, 17 (11.7%) had thrombotic closures. Intracoronary
thrombolytic therapy was administered, and repeat coronary balloon dilation was performed in all patients. Successful recanalization was achieved in only 7 patients (41%); 13 had an acute myocardial infarction, and 8 were referred for coronary bypass surgery. Foley et al. (5) reported their experience with Palmaz-Schatz stent implantation in 160 consecutive patients: Stent thrombosis occurred in 12 patients (7.5%), 10 of whom were treated with angioplasty with or without intracoronary thrombolytics. Patency was restored in 50% of patients treated with angioplasty. Haude et al. (3) described 100 consecutive patients with intracoronary implantation of 118 Palmaz-Schatz stents, 10 (10%) of whom developed subacute stent thrombosis. In contrast to the previously described studies, eight of the nine patients managed with catheter-based therapies had flow restored. The discrepancies in outcome among the different studies could possibly be explained in part by patient selection, stent type, indication for stenting, operator experience and perhaps the use or nonuse of intracoronary thrombolytic therapy. However, common to all these studies is a high rate of severe adverse clinical outcomes despite revascularization attempts.

Thrombus. Primary angioplasty has been advocated by some as the therapy of choice for acute myocardial infarction because of high success rates and improved clinical outcomes compared with thrombolytic therapy (17,18). Because intracoronary thrombus is common to acute myocardial infarction and stent thrombosis, it is of interest that angioplasty appears to be of much lower efficacy in restoring flow and resolving residual thrombus in the latter condition. Our data, as well as previous data (2,5), indicate that thrombolytic therapy adjunc- tive to angioplasty is of limited efficacy in resolving residual thrombus formation within the stent site and possibly could even be harmful. In fact, Ambrose et al. (10) recently reported that adjunctive intracoronary urokinase during angioplasty of thrombus-containing lesions in patients with unstable angina is associated with adverse angiographic and clinical events, perhaps because of platelet-activating effects of urokinase. One can only speculate as to the different mechanisms for thrombus formation in these two situations and how this affects treatment with thrombolytic agents. It is possible that even higher doses or prolonged infusions of thrombolytic agents might be more effective for treatment of stent thrombosis, as reported for treatment of occluded venous grafts (19,20), but this could also be associated with a significantly higher complication rate, and substantially prolonged instrumentation of the vessel containing a stent is probably best avoided to prevent further complications. Alternatively, it is possible that the thrombus that forms within the intracoronary stent is resistant to thrombolytic agents.

Analysis of the thrombus composition in a porcine experimental model of stent thrombosis has revealed that it is platelet-rich in content (21). Indeed, a postmortem study of one of our patients who died after treatment with angioplasty and intracoronary urokinase infusion revealed acute platelet fibrin thrombotic occlusion of stent sites with platelet-fibrin emboli within small intramural coronary arteries (Fig. 2). Because thrombolytic agents exert their effect primarily by fibrinolysis, they may be expected to have limited efficacy in resolving platelet-rich thrombi (22). Moreover, the efficacy of thrombolytic agents may be blunted by the high content of plasminogen activator inhibitor in these thrombi (23). It remains to be determined whether alternative adjunctive antiplatelet agents such as platelet glycoprotein IIb/IIIa receptor antagonists or antithrombin agents such as hirudin can improve clinical outcome among patients with early stent thrombosis.

The great majority of patients with stent thrombosis in our series were receiving warfarin at the time of stent occlusion. Most of these patients were well anticoagulated, with INR values >2, or were receiving concomitant infusion of heparin with adequate activated partial thromboplastin time values (>70 s). Thus, it is apparent that adequate anticoagulation with warfarin does not prevent the occurrence of early stent thrombosis. Indeed, warfarin may promote a procoagulant state because of its initial inhibitory effects on the anticoagulants proteins C and S, as implicated in other thrombotic diatheses (24). However, the potential contribution of warfarin to the thrombotic episodes in stent recipients remains speculative.

In our series of patients, we observed a relatively high rate of referral for coronary bypass surgery despite restoration of antegrade flow. These patients had angiographic evidence of residual thrombus and experienced refractory angina. There are few other data regarding the outcomes of patients with stent thrombosis and restored flow with residual thrombus. Although all patients in our study referred for urgent or emergent coronary bypass surgery after angioplasty because of residual thrombus fared well, it is possible that medical therapy may have also been successful.

Study limitations. The present study was a retrospective analysis of different stent types and different technical approaches to stent deployment. Follow-up of patients receiving intracoronary stents in our institution was complete, and although it is unlikely that symptomatic events were missed, we cannot exclude the possibility that silent stent thrombosis might have been missed. In addition, because of the small number of patients receiving a particular therapeutic modality, and because the choice of the therapeutic approach was at the discretion of the operator, it is not possible to assess differences in outcome with different therapeutic approaches. It should also be emphasized that it was not the goal of this study to describe predictors of early stent thrombosis occurrence but rather to provide insight into the clinical course of patients with stent thrombosis and evaluate the efficacy of commonly used therapeutic strategies. Last, high pressure balloon inflations were not routinely performed during treatment of stent thrombosis. It is possible that higher inflation pressures, perhaps with larger balloons, and verification of adequate stent apposition with intravascular ultrasound might have resulted in better resolution of residual thrombus.

Conclusions. Initial experience with intracoronary stents resulted in relatively high complication rates (1-5), which
improved dramatically over time with improved technical expertise, patient selection and adjunctive therapy (6). However, as more experience with stent implantation is gained, patients with increasingly complex clinical and angiographic profiles may be treated. In addition, the use of stents in interventional cardiology practice worldwide continues to grow rapidly. Thus, the rate of stent thrombosis may actually increase over time, and the absolute number of cases even more so.

In our series of patients treated with coronary stent placement, early stent thrombosis was associated with high rates of adverse clinical outcomes. Catheter-based therapies were successful in restoring normal flow but were of modest efficacy in the management of these patients because of the high incidence of associated adverse clinical events. It is therefore imperative to formulate more effective treatment strategies for early stent thrombosis.

We thank LaVonne Hammes for invaluable help with data collection.

References


