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Intracoronary Stenting Without Anticoagulation Accomplished With Intravascular Ultrasound Guidance

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Abstract

Background The placement of stents in coronary arteries has been shown to reduce restenosis in comparison to balloon angioplasty. However, clinical use of intracoronary stents is impeded by the risk of subacute stent thrombosis and complications associated with the anticoagulant regimen. To reduce these complications, the hypothesis that systemic anticoagulation is not necessary when adequate stent expansion is achieved was prospectively evaluated on a consecutive series of patients who received intracoronary stents.

Methods and Results From March 1993 to January 1994, 359 patients underwent Palmaz-Schatz coronary stent insertion. After an initial successful angiographic result with <20% stenosis by visual estimation had been achieved, intravascular ultrasound imaging was performed. Further balloon dilatation of the stent was guided by observation of the intravascular ultrasound images. All patients with adequate stent expansion confirmed by ultrasound were treated only with antiplatelet therapy (either ticlopidine for 1 month with short-term aspirin for 5 days or only aspirin) after the procedure. Clinical success (procedure success without early postprocedural events) at 2 months was achieved in 338 patients (94%). With an inflation pressure of 14.9±3.0 atm and a balloon-to-vessel ratio of 1.17±0.19, optimal stent expansion was achieved in 321 of the 334 patients (96%) who underwent intravascular ultrasound evaluation, with these patients receiving only antiplatelet therapy after the procedure. Despite the absence of anticoagulation, there were only two acute stent thromboses (0.6%) and one subacute stent thrombosis (0.3%) at 2-month clinical follow-up. Follow-up angiography at 3 to 6 months documented two additional occlusions (0.6%) at the stent site. At 6-month clinical follow-up, angiographically documented stent occlusion had occurred in 5 patients (1.6%). At 6-month clinical follow-up, there was a 5.7% incidence of myocardial infarction, a 6.4% rate of coronary bypass surgery, and a 1.9% incidence of death. Emergency intervention (emergency angioplasty or bailout stent) for a stent thrombosis event was performed in 3 patients (0.8%). The overall event rate was relatively high because of intraprocedural complications that occurred in 16 patients (4.5%). Intraprocedural complications, however, decreased to 1% when angiographically appropriately sized balloons were used for final stent dilations. There was one ischemic vascular complication that occurred at the time of the procedure and one ischemic vascular complication that occurred at the time of angiographic follow-up. By 6 months, repeat angioplasty for symptomatic restenosis was performed in 47 patients (13.1%).

Conclusions The Palmaz-Schatz stent can be safely inserted in coronary arteries without subsequent anticoagulation provided that stent expansion is adequate and there are no other flow-limiting lesions present. The use of high-pressure final balloon dilatations and confirmation of adequate stent expansion by intravascular ultrasound provide assurance that anticoagulation therapy can be safely omitted. This technique significantly reduces hospital time and vascular complications and has a low stent thrombosis rate.

Key Words:
- stents
- ultrasonics
- balloon
- platelets

The placement of intracoronary stents decreases the morbidity of acute closure and reduces the restenosis rate in de novo lesions and vein grafts compared with historical angioplasty results. More recently, the Benestent and STRESS randomized trials compared stents and angioplasty in treating de novo native coronary artery lesions. Both studies demonstrated a significant reduction in the restenosis rate in the group treated with stents. In addition, in the Benestent trial, the reduction in restenosis rate was associated with a significant reduction in major clinical events in the group randomized to stents. Increased clinical use of stents may be justified on the basis of these investigations but is impeded by two major limitations: the risk of stent thrombosis and the complications associated with an aggressive anticoagulation regimen. A stringent anticoagulation regimen has been advocated to inhibit the incidence of subacute stent thrombosis but is associated with bleeding and vascular complications without eliminating subacute stent thrombosis.

Prior studies with intravascular ultrasound imaging of deployed stents reveal that >80% of stents may be insufficiently dilated despite an apparently angiographically successful deployment. These observations suggest that stent thrombosis may be caused in part by incomplete stent dilatation rather than the inherent thrombogenicity of the metallic stent.
The hypothesis of this study is that systemic anticoagulation is not necessary after stent insertion when adequate stent expansion is achieved. This hypothesis was prospectively evaluated in a consecutive series of 359 patients who received Palmaz-Schatz intracoronary stents. All patients with adequate stent expansion as confirmed by intravascular ultrasound were treated only with antiplatelet therapy and did not receive anticoagulation after the procedure.

Methods

Between March 30, 1993, and January 1, 1994, 359 consecutive patients with 452 lesions were treated with insertion of a Palmaz-Schatz intracoronary stent. During the first 3 months of this investigation, patients were informed of the potential risks and benefits of intracoronary stents and of the novelty of the approach used in this investigation and consented to participate in the study. After the first 3 months, consent was obtained after patients were informed of the risk and benefit of intracoronary stents and of the interim results of this protocol compared with the outcome of stenting with standard anticoagulation regimens. The first 10 patients enrolled in the study were selected on the basis of having lesions that were at low risk of causing major ischemic complications in the event of a stent occlusion (eg, total occlusion lesions, non-left anterior descending lesions, or lesions supplying a small or modest amount of myocardium). Subsequent to this selection, there was no attempt to limit enrollment in patients who consented and met inclusion criteria. The entry criteria included (1) coronary artery disease manifested by clinical symptoms or objective evidence of myocardial ischemia either on exercise test or by nuclear scintigraphy and (2) angiographic evidence of single- or multiple-vessel coronary disease with target lesion stenosis >70% by visual estimate. The exclusion criteria included (1) small vessels <2.5 mm by visual estimate and (2) angiographically diffuse distal disease that might compromise outflow after stent insertion. There were no specific age or ejection fraction limitations for study entry. Patients were not excluded on the basis of indication for stent implantation, lesion location, or complex lesion morphology. Thus, patients with ostial lesions, tortuous vessels, diffuse disease, long lesions, tandem lesions, and lesions with thrombus or severe calcification were eligible for study entry.

Stent Implantation Procedure

Patients received aspirin 325 mg and calcium channel antagonists before stent deployment. A bolus of 10 000 U heparin was given after sheath insertion, with a repeat bolus of 5000 U given as needed to maintain the activated clotting time >250 seconds. Patients were not given dextran or dipyridamole before, during, or after the stent procedure. Ticlopidine was not administered before or during the stent procedure. Five different types of Johnson and Johnson tubular slotted stents were used during the course of this study: the Palmaz-Schatz stent, a short stent composed of one 7-mm tubular slotted segment, a 10-mm-long biliary stent, a 20-mm renal-stent composed of two 10-mm segments with a central articulation, and a short (disarticulated) renal stent. A premounted stent delivery system was used sparingly during the study (n=7). After predilation, stents were hand crimped on balloons and implanted under fluoroscopic guidance. Further dilatations (angiographic optimization) were performed to achieve an acceptable angiographic result with <20% residual stenosis by visual estimates. After the angiographic result was considered acceptable and the procedure would ordinarily be terminated, intravascular ultrasound was performed. All subsequent treatment decisions were based on the ultrasound results in conjunction with angiographic assessment. The initial intravascular ultrasound was the first ultrasound examination performed when initial angiographic success (<20% residual stenosis by visual estimate) was achieved. The final intravascular ultrasound was the last intravascular ultrasound evaluation, which were documented that the criteria for stent expansion were achieved. Further balloon dilatation or stent implantation that was performed after the initial intravascular ultrasound imaging was called intravascular ultrasound-guided stent optimization.

The indicators for placement of stents were defined as follows: Acute occlusion stenting was undertaken to relieve ischemia associated with complete vessel closure (100%) after angioplasty with no or markedly delayed grade 0 or 1 Thrombolysis in Acute Myocardial Infarction (TIMI) flow; threatened closure stenting was performed when the angioplasty was complicated by a longitudinal or spiral dissection associated with >50% luminal encroachment (with or without compromised flow) and evidence of ischemia; suboptimal result stenting was defined as insertion of a stent for a focal dissection or significant vascular recoil after angioplasty that resulted in >50% luminal narrowing but was not associated with ischemia; restenosis stenting was performed for lesions with a history of restenosis after one or more previous angioplasty procedures; chronic occlusion stenting was performed after a vessel that had been occluded for more than 2 months was reopened; and elective stenting was performed when the operator believed a better result would be obtained with a stent instead of balloon angioplasty. Multiple stenting was defined as the use of more than one Palmaz-Schatz (15-mm) stent. Short stents were counted as a half stent. Biliary, disarticulated renal, and renal stents were counted as one stent each.

Intravascular Ultrasound Equipment and Measurements

The majority of coronary arteries were imaged with a 3.9F monorail system with a 25-MHz transducer-tipped catheter (Interpret Catheter, InterTherapy/CVIS). A Cardiovascular Imaging System (CVIS) with a 2.9F catheter was used during the last 3 months of the study. Validation of quantitative measurements and pathological correlation with ultrasound measurements has been reported. All images were obtained with a manual pullback system. The position of the catheter on fluoroscopy was used to correlate the ultrasound image with the angiogram. Data were stored on 0.5-in. super VHS videotape. On-line quantitative measurements were performed during the procedure. The ultrasonic catheter was advanced distal to the stent, and images were recorded while the imaging catheter was slowly pulled through the stented segment. The following measurements were made at the proximal or distal reference sites, generally within 5 to 10 mm of the stented segment: vessel cross-sectional area (CSA), vessel minimal and maximal diameters, lumen CSA, and lumen minimal and maximal diameters. The reference site measurements were made at sites that did not appear severely diseased on intravascular ultrasound image and that had a minimum of balloon trauma from prior balloon dilatation. Thus, these measurements were thought to be a reasonable and practical reflection of the true lumen or vessel size by intravascular ultrasound. The border of the vessel (as distinguished from the lumen) was defined on the ultrasound image as the outer boundary of the echolucent medium surrounding the plaque. Lumen measurements were made at the inner border of the echo-dense plaque. Intrastent lumen CSA and diameter measurements were made at the tightest position within the stent. The average of the proximal and distal vessel CSAs was used to estimate the vessel dimensions of the stented segment because intense echo reverberations from the metallic struts frequently prevented measurements of the vessel boundary beyond the stent. Intravascular ultrasound imaging was performed in the reference sites and in the stented segment at the initial intravascular ultrasound evaluation and after each series of balloon dilations. Measurements were made at the tightest point within the stented segment after each series of balloon dilations. The measurements at the reference site were done on the initial intravascular ultrasound evaluation to minimize the potential balloon dilatation effect that might increase the dimensions of the reference site.
Interobserver and intraobserver reproducibility of minimum lumen diameter and lumen CSA measurements was retrospectively evaluated by linear regression analysis. Interobserver reproducibility was assessed by two senior angiographers (S.N. and P.H.) performing blinded measurements of randomly selected stent sites (n=30) and reference segments (n=30). Intraobserver reproducibility was based on blinded measurements performed at a different time. The reproducibility of the measurements was reported as correlation coefficients.\textsuperscript{2} Interobserver correlation coefficients for the minimal lumen diameter and lumen CSA measurements at the stent site were 0.94±0.14 mm and 0.97±0.50 mm\textsuperscript{2}, and intraobserver correlation coefficients were 0.96±0.13 mm and 0.98±0.43 mm\textsuperscript{2}. In reference segments, interobserver correlation coefficients of the minimum lumen diameter and lumen CSA measurements were 0.93±0.23 mm and 0.98±0.64 mm\textsuperscript{2}, and intraobserver correlation coefficients were 0.93±0.23 mm and 0.99±0.38 mm\textsuperscript{2}. Interobserver correlation coefficients for the reference minimum vessel diameter and vessel CSA were 0.98±0.16 mm and 0.99±0.46 mm\textsuperscript{2}, and intraobserver correlation coefficients were 0.98±0.15 mm and 0.99±0.38 mm\textsuperscript{2}. All probability values were significant to <.0001.

**Intravascular Ultrasound Criteria for Optimal Stent Expansion**

The criteria for optimal stent expansion were governed by the principles of optimizing stent expansion and covering the full extent of the lesion so as to minimize any potential impairment to flow that could contribute to stent thrombosis. The first criterion was a qualitative evaluation of the stent site involving the achievement of good stent apposition to the vessel wall with good plaque compression. The second criterion was the achievement of a quantitative assessment of optimal stent expansion. During the course of the investigation, two quantitative criteria for stent expansion were used. For the majority of the lesions (n=339), 60% of the average of the proximal and distal CSAs was the target for defining intravascular ultrasound success.\textsuperscript{25} This target criterion was initially chosen to accommodate the compensatory dilation that occurs with early atheroma deposition, an observation that has been made in both morphology and intravascular ultrasound investigations even in the angiographically normal reference site.\textsuperscript{23, 26, 27} The quantitative criterion for optimal stent expansion was altered in the last 113 lesions so that the goal was to achieve an intrastent lumen CSA equal to or greater than the distal reference lumen CSA. The quantitative criterion for assessing optimal stent expansion was adjusted during the course of the investigation to simplify the criterion and because of the perceived overriding importance of not leaving the stent with a stenosis relative to the distal lumen rather than achieving a specified percent dilation relative to the reference vessel. A third (and equally important) ultrasound criterion was that the nonstented segments immediately adjacent to the stent (proximal or distal) did not reveal evidence of a significant lesion defined as a CSA stenosis >60% relative to the adjacent reference lumen. This criterion was established in an attempt to apply a simple and consistent quantitative measurement that could be used to judge and treat lesions that were occasionally seen at the stent margin or in adjacent unstented segments. When a significant lesion was observed in these segments, angioplasty or, more commonly, stent implantation was performed. These lesions were categorized as residual plaque or fractured plaque. A final criterion involving the achievement of symmetrical stent expansion was also one of the initial criteria as previously reported but was never used independently of CSA measurements and was shown in previous intravascular ultrasound studies to not change significantly during stent optimization.\textsuperscript{22, 25} This, the use of this criterion was abandoned.

**Balloon Dilatation and Stent Implantation Strategy**

The approach to stent expansion evolved during the study. In the initial 339 lesions, the balloon for final dilatations was sized close to the intravascular ultrasound vessel major diameter. The final stent balloon dilatations were performed with minimally compliant short balloons (generally the 9-mm Chubby, Schneider). This strategy translated into performing final balloon dilatations with balloons oversized by visual estimate of the angiogram. Moderate maximal inflation pressures (8 to 14 atm) were used in the first 40 lesions, and subsequently, high maximal inflation pressures (>14 atm) were used for the final balloon dilatation. In the final 113 lesions, final stent dilatations were performed with a balloon more appropriately sized to the angiographic vessel diameter by visual estimate when inflated to high maximal pressures. In this phase, final balloon dilatations were performed with noncompliant balloons (NC Shadow, SCIMED Life Systems) inflated to pressures up to 20 atm.

**Angiographic Analysis**

Coronary angiograms were analyzed without knowledge of the intravascular ultrasound data by experienced angiographers not involved in the stenting procedure. Patients received intracoronary nitroglycerin before baseline and final angiograms to achieve maximal vasodilation. To optimize reproducibility, the position of the x-ray gantry was recorded in all views at the time of the baseline angiograms, and final angiograms were done in matching views. Angiographic measurements were made during diastole. The lesions were measured with digital calipers (Brown and Sharp) from an optically magnified image in a single, matched “worst” view. The guiding catheter was used as the reference object for magnification calibration. Previous studies have shown that digital calipers correlate closely with computer-assisted methods, with a low interobserver and intraobserver variability.\textsuperscript{28, 29} Minimal lumen diameter and percent diameter stenosis were obtained on the baseline and final angiograms. The diameters of the proximal and distal lumen reference sites were averaged to obtain a mean reference diameter. The average reference diameter was used to calculate the percent diameter stenosis at baseline and final angiogram. The average reference diameter was used for these calculations to have a correlation with the proximal and distal measurements performed on intravascular ultrasound and also because the average reference vessel was thought to be a better reflection of the vessel size when multiple stents were placed in long segments that were of varying diameter. Lesion length was measured on baseline angiography from the point at which the lumen was compromised by 50% at the proximal or distal reference vessel site. Lesions were characterized according to the modified American College of Cardiology-American Heart Association (ACC/AHA) score.\textsuperscript{30} The distance between lesions in the same vessel was measured. Tandem lesions were defined as lesions in the same vessel that were separated by <15 mm. Long lesions were defined as a single continuous narrowing >15 mm. The presence of large filling defects was noted at baseline or during the procedure. Thrombus was defined as a filling defect seen in multiple projections surrounded by contrast in the absence of calcification. TIMI grade flow was recorded at the time of the initial procedure to characterize the indication for stenting as previously described.\textsuperscript{31} Angiographic findings such as the occurrence of dissection, vessel rupture, or side branch compromise were recorded and analyzed.

**Events**

Major clinical events were considered death, emergency bypass surgery, elective bypass surgery, myocardial infarction (Q-wave or non–Q-wave), emergency repeat intervention (bail-out stenting or repeat angioplasty), and vascular complications. Specific major event definitions were as follows: Death was defined as any death irrespective of cause. A diagnosis of Q-wave myocardial infarction was made when there was documentation of new pathological Q waves (<0.14 seconds) on an ECG in conjunction with elevation of creatine kinase to greater than twice the upper limit of normal. A diagnosis of non–Q-wave myocardial infarction was defined as elevation of the cardiac enzymes to greater than twice the upper limit of normal
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Palmaz-Schatz stents were implanted in 132 lesions (29%). Two short stents were placed in 234 lesions (52%). One Palmaz-Schatz stent and one short stent were deployed in 50 lesions (11%). Two or more vessel 1.72±1.14, and per patient 1.8±1.17. A single short stent was placed in 36 lesions (8%). A single Palmaz-Schatz stent (one Palmaz-Schatz or 398 vessels (49%), and in 199 of 359 patients (55%). The mean number of stents per lesion was 1.51±0.98 (range, 0.5 to 9 stents per lesion), per patient 1.72±1.14, and per patient 1.8±1.17. A single short stent was placed in 36 lesions (8%). A single Palmaz-Schatz stent (one Palmaz-Schatz or two short stents) was placed in 234 lesions (52%). One Palmaz-Schatz stent and one short stent were deployed in 50 lesions (11%). Two or more Palmaz-Schatz stents were implanted in 132 lesions (29%).

Events were categorized as intraprocedural complications, postprocedure events that occurred during hospitalization (hospital events), events that occurred after hospital discharge up to 2 months (short-term posthospitalization events), and late events that occurred between 2 and 6 months of clinical follow-up. Cumulative events were reported at 6-month clinical follow-up. Intraprocedural and early postprocedural events were separated to evaluate the safety of the intravascular ultrasound-guided stent implantation procedure and to assess the efficacy of antiplatelet therapy without anticoagulation after a successful stent procedure.

Postprocedure Medication Protocol

If the intravascular ultrasound criteria for optimal stent expansion were met and the angiographic result was also acceptable, no further heparin was administered and sheaths were removed in 4 to 6 hours. When procedures were performed in the evening, heparin was infused overnight and the sheaths were removed the following morning. The first 252 patients to complete a successful Palmaz-Schatz stent procedure received ticlopidine 250 mg PO BID for 2 months (the first 150 patients) or 1 month (subsequent 102 patients). Patients who had not received ticlopidine before the stent procedure also received aspirin 325 mg/d for 3 to 5 days. The last 69 consecutive patients in this cohort were treated only with aspirin 325 mg BID.

Patients who did not have intravascular ultrasound performed, patients who had an attempted but unsuccessful intravascular ultrasound evaluation, and patients who had a final suboptimal intravascular ultrasound performed were treated with a standard postprocedure anticoagulation and antiplatelet regimen. In these patients, at the completion of the stent procedure, the heparin was discontinued briefly to allow for sheath removal, then reintroduced within 4 to 6 hours. Warfarin was initiated on the day of the procedure, and both heparin and warfarin were continued until the prothrombin time was >16 (international normalized ratio, 2.0 to 3.5), after which the heparin was stopped. Starting on the day of the procedure, these patients received aspirin 325 mg/d indefinitely but did not receive dextran or dipyridamole.

Follow-up

In the first 2 months of this protocol (first 60 patients), patients were observed in the hospital for 7 to 10 days. Subsequently, patients were discharged from the hospital within 2 days. This was done so that an evaluation of the safety and efficacy of short hospitalizations after stent implantation could also be performed. The short-term complications (stent thrombosis) continued to be carefully assessed with regular and uniform contact of all patients within 4 weeks of hospital discharge and at 2 months. Late clinical follow-up was performed at 6 months.

Statistics

Normally distributed data are expressed as mean±SD. Data that are not normally distributed are expressed as a median with a range of values. Comparisons between equivalent groups were performed by paired Student’s t test. Subgroup comparisons of discrete variables were made by χ² analysis. Differences were considered statistically significant at P<.05. Intraobserver and interobserver reproducibility of minimum lumen diameter and lumen CSA measurements were evaluated by linear regression analysis.

Results

Patient, Angiographic, and Procedural Characteristics

The clinical characteristics and indications for use of a stent in the 359 patients undergoing Palmaz-Schatz stent implantation are shown in Table 1. The majority of stent procedures were performed electively (67%). Angiographic and procedural characteristics are presented in Table 2. A total of 452 lesions were treated in 398 vessels. A total of 864 stents were implanted. Multiple stents were implanted in 180 of 452 lesions (40%), in 196 of 398 vessels (49%), and in 199 of 359 patients (55%). The mean number of stents per lesion was 1.51±0.98 (range, 0.5 to 9 stents per lesion), per vessel 1.72±1.14, and per patient 1.8±1.17. A single short stent was placed in 36 lesions (8%). A single Palmaz-Schatz stent (one Palmaz-Schatz or two short stents) was placed in 234 lesions (52%). One Palmaz-Schatz stent and one short stent were deployed in 50 lesions (11%). Two or more Palmaz-Schatz stents were implanted in 132 lesions (29%).
Between March 30, 1993, and January 1, 1994, a total of 359 consecutive patients with 452 lesions underwent intracoronary stent implantation. After stent deployment and angiographic optimization, initial stent implantation was successful in 347 patients (96.6%) and in 438 lesions (96.9%), as shown in Fig 1. Before intravascular ultrasound imaging, stent implantation was unsuccessful in 12 patients (3.3%) with 14 lesions (3.1%). After initial stent implantation success, there were 9 patients (2.6%) with 13 lesions (2.9%) that did not have intravascular ultrasound performed for technical reasons, and intravascular ultrasound was unsuccessful in 3 patients (0.8%) with 5 lesions (1.1%). Of the 420 lesions in 335 patients that were imaged by intravascular ultrasound, optimal stent expansion was observed in 127 lesions (30%) on the initial ultrasound evaluation. After intravascular ultrasound-guided stent site optimization, a final optimal ultrasound result was achieved at the stent site on 402 lesions (96%) in 321 patients (96%). With increased experience and the change in the criteria for success, the percent of lesions in which there was adequate stent expansion at the initial intravascular ultrasound increased from 12% in the first 100 lesions to 60% in the last 113 lesions. During the process of intravascular ultrasound-guided optimization, stent failure with major complications occurred in an additional 6 patients (1.7%) with 8 lesions (1.7%).

There were 8 patients (2.2%) with 10 lesions (2.2%) who had a suboptimal stent result at the final intravascular ultrasound evaluation. The 321 patients who had adequate stent expansion by intravascular ultrasound criteria were treated with antiplatelet medications and did not receive additional anticoagulation (heparin or warfarin). During the 2-month short-term clinical follow-up, there were three stent thrombosis events in the 321 patients (0.9%) with 399 lesions (0.7%) treated only with antiplatelet therapy and no anticoagulation. The short-term clinical follow-up was done in all patients at 2 months. An additional two stent occlusions (0.6%) were documented at angiographic follow-up at 3 and 4 months. These occlusions were associated with angina recurrence but not clinical events.

A total of 20 patients (5.6%) were treated with a standard anticoagulation regimen consisting of short-term heparin, warfarin for 2 months, and aspirin indefinitely. This group included the 9 patients who did not have intravascular ultrasound guidance, the 3 patients who had an attempted but unsuccessful intravascular ultrasound procedure, and the 8 patients who had a final intravascular ultrasound that revealed suboptimal stent expansion. These patients did not have any clinical or angiographically documented stent thrombosis events.

Unsuccessful Stent Implantation and Intraprocedural Events

The stent implantation procedure was unsuccessful in 18 patients (5.0%). Two of the procedures were unsuccessful without clinical events. Unsuccessful stent implantation associated with a major event occurred in 16 patients (4.5%), as shown in Table 3. In these 16 patients, myocardial infarction occurred in 11 patients (3.1%), only 5 of whom had Q-wave myocardial infarctions (1.4%). Emergency bypass was necessary in 11 patients (3.1%) and elective bypass in 2 patients (0.6%). Three patients (0.8%) died during the procedure. The timing of the 18 unsuccessful stent implantation procedures relative to the intravascular ultrasound imaging is illustrated in Fig 1. Successful stent implantations associated with major clinical events were due to unsuccessful stent delivery in 5 patients (1.4%) and occurred after successful stent delivery to the lesion site in 11 patients (3.1%), as shown in Fig 2. Unsuccessful stent delivery was due to incomplete lesion coverage in 3 patients, left main dissection from guiding catheter trauma before stent delivery in 1 patient, and left anterior descending artery dissection that occurred during stent delivery into an angulated circumflex in 1 patient. Causes of complications after successful stent delivery included distal embolization in a degenerated vein graft in 1 patient and dissection from the intravascular ultrasound catheter in one patient. After successful stent delivery, stent site optimization complications were nonocclusive dissections in 4 patients (1.1%), coronary vessel rupture in 4 patients, and side branch compromise during stent optimization in 1 patient.

Table 3.

| Intraprocedural, Hospital, Early Posthospitalization (≤2 Months), Late (2 to 6 Months), and Cumulative Events at 6-Month Follow-up |

[View this table:](#)
Early Postprocedural Events

Early postprocedural hospital events occurred in 4 patients (Table 3†). Two patients had acute thrombosis events at the stent site 3 hours and 12 hours after the stent procedure. Both of these events were associated with Q-wave myocardial infarctions. One of the acute occlusions occurred in the vessel with slow flow related to a preexistent coronary Rotablator procedure. The second acute thrombosis event was the result of a vessel closure distal to a patent stent that had preserved flow into a large side branch. While not strictly a stent thrombosis, the occlusion was counted as an acute thrombosis event because the distal dissection was a result of the stent implantation procedure. This patient underwent bailout stent implantation, which restored vessel patency and hemodynamic stability before emergency coronary bypass surgery. One other non-Q-wave myocardial infarction occurred in the postprocedure hospitalization period that was not due to stent thrombosis. This patient had undergone a combined Rotablator and stent procedure and returned to the catheterization laboratory for angiographic evaluation of an asymptomatic cardiac enzyme elevation. Angiographic and intravascular ultrasound evaluations revealed a patent stent site and no evidence of thrombus. This non-Q-wave myocardial infarction event was considered an embolic event related to a preexistent Rotablator procedure.

After the procedure, there were one vascular complication and one death, in the same patient. This patient underwent multiple percutaneous interventions and vascular surgical repairs for lower-extremity ischemia, developed rhabdomyolysis and renal failure, and died 17 days after the stent procedure of multiorgan failure and sepsis.

Short-term clinical follow-up was obtained in all patients at 2 months. During the 2-month short-term clinical follow-up period after hospital discharge, there was one subacute stent thrombosis event (Table 3†). The event occurred 8 days after the stent procedure and was associated with a non-Q-wave myocardial infarction. The occlusion was reopened, an additional bailout stent was placed at the site of a distal dissection, and the patient continued on antiplatelet therapy.

Late Events

Long-term follow-up was obtained in 351 patients (98%). Late events between 2 and 6 months occurred in 57 patients (16%), as shown in Table 3†. The majority of these events were repeat angioplasty, performed in 47 patients (13.1%) for symptomatic restenosis. A total of 8 patients (2.2%) underwent nonemergency coronary bypass during the late follow-up period. Myocardial infarction during the late follow-up was observed in 5 patients (1.4%). There were 3 deaths during the late follow-up period, and all were cardiac related. One death occurred after a large inferior myocardial infarction in a patient 5.5 months after stent implantation in the left anterior descending artery. An angiogram performed 3 weeks before the death revealed a patent left anterior descending artery stent and moderate diffuse disease in the right coronary artery but no evidence of a critical lesion. A second late death was a witnessed in-hospital ventricular fibrillation event 4 months after the procedure. The patient had a history of ischemic cardiomyopathy and refractory ventricular arrhythmias. The third late death also occurred in a patient with ischemic cardiomyopathy due to refractory congestive heart failure without evidence of ischemia.

Angiographic Analysis

As shown in Table 4, the baseline proximal reference vessel diameter was 3.3±0.53 mm. The baseline distal reference vessel was 3.06±0.56 mm. The baseline average (of proximal and distal) reference vessel diameter was 3.18±0.53 mm. The reference vessel diameter after the stent procedure was not significantly different. Baseline minimum lumen diameter was 0.94±0.57 mm, with a baseline percent diameter stenosis of 71±16%. The final stent diameter was 3.39±0.53 mm, with a mean final percent stenosis of −7±16%. Mean lesion length was 9.5±6.7 mm. The median length of the lesions was 7.6 mm (range, 1.2 to 39 mm). The results were achieved with a mean pressure of 14.9±3.0 atm and a balloon-to-vessel ratio of 1.17±0.19.

Table 4.
Quantitative Angiographic Measurements

<table>
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<th>Measurement</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area (mm²)</td>
<td>2.92±0.82</td>
</tr>
<tr>
<td>Stenosis (%)</td>
<td>67±15</td>
</tr>
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Qualitative angiographic assessment revealed other information on the effect of high-pressure balloon dilatation. Transient side branch occlusion during the stent procedure occurred in 15 lesions (3.3%). These transient occlusions usually resolved with the administration of intracoronary nitroglycerin but sometimes required balloon dilatation. All had resolved at the end of the stent procedure and were not associated with major events. Vasospasm was noted more prominently during the procedure when high pressures, >15 atm, were used for final balloon dilation. This phenomenon was self-limiting, always resolved with time or after high doses of intracoronary nitroglycerin, and was not associated with any unfavorable clinical events.

Intravascular Ultrasound Analysis

Table 5‡ shows the intravascular ultrasound measurements. The mean lumen CSA at the tightest point within the stent increased 26% from 6.5±2.0 mm² at the initial intravascular ultrasound to 8.8±2.5 mm² at the final intravascular ultrasound (P<.0001). The tightest intrastent lumen area relative to the reference area expanded from 49±13% at the initial intravascular ultrasound to 66±13% at the final intravascular ultrasound (P<.0001). The minor stent lumen diameter increased from 2.7±0.5 to 3.1±0.5 mm (P<.0001), and the major stent diameter increased from 3.1±0.5 to 3.5±0.5 mm between the initial and final intravascular ultrasound (P<.0001). A mean of 2.4±1.2 ultrasound evaluations were performed per lesion. Examples of suboptimal stent expansion with subsequent intravascular ultrasound-guided stent optimization are shown in Figs 3‡ and 4‡.

Figure 3.
Example of intravascular ultrasound–guided coronary stent implantation. A, Baseline angiogram of a left anterior descending artery with a proximal stenosis (arrow). B, Angiogram after stent deployment (between open white triangles) and initial dilatation with 3.5-mm balloon...
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Stent struts are demarcated by black-and-white arrows and the stenosis relative to $P_2$, was smaller than $P$. Additional stents were inserted at these sites, a 66% increase from the initial intravascular ultrasound image.

After further high-pressure dilatation, the stent CSA increased to 11.7 mm$^2$. The initial stent CSA of 4.6 mm$^2$ was smaller than the distal lumen CSA of 8.5 mm$^2$. After further high-pressure dilatation, the stent CSA increased to 11.7 mm$^2$, and the stenosis relative to the distal lumen was obliterated.

**Effect of Antiplatelet Therapy**

In the 252 patients treated with ticlopidine, there were two acute stent thromboses (0.8%). In the 69 patients treated with aspirin alone after the stent procedure, there was one subacute stent thrombosis (1.4%). There was no significant difference between the stent thrombosis rates between the ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5 ticlopidine and the aspirin treatment groups. Side effects that precipitated medication discontinuation were more frequent with ticlopidine than with aspirin. Ticlopidine was stopped for minor complications of skin rash or gastrointestinal disturbances within 2 weeks of the stent insertion in 5
patients. Neutropenia was documented in 2 patients and was reversible after the medication was stopped. These 7 patients were continued on aspirin after the ticlopidine was discontinued. There were no adverse medication effects in the 69 patients treated with aspirin.

Discussion

The results of this nonrandomized study on patients undergoing intravascular ultrasound-guided intracoronary stent implantation indicate that anticoagulation can be safely withheld when adequate stent expansion is achieved and flow optimized in the stented and adjacent inflow and outflow segments. These findings represent a departure from previous doctrine regarding coronary stents and suggest an alternative approach that may eliminate the need for anticoagulation, with reduction in hospital stay and vascular complications.

Comparison With Other Studies

Large multicenter studies on patients undergoing elective stenting have reported an incidence of stent thrombosis of 3% to 4%. Hospital or early complications included a 3% incidence of Q-wave myocardial infarction, a 2% to 3% rate of non-Q-wave myocardial infarction, and a 2% to 3% need for bypass surgery. When stenting is performed for bailout or emergency indications, stent thrombosis and major complication rates are higher. The incidence of stent thrombosis is 8% to 16% with a 6% to 21% rate of myocardial infarction, a 4% to 13% need for emergency bypass surgery, and a 2% to 4% incidence of death. Although stents decrease morbidity of acute closure, lower the incidence of major hospital or early events, and reduce restenosis rates compared with angioplasty-treated groups, the potential benefit of stent implantation is, unquestionably, lost in patients with stent thrombosis.

Vascular access complications and bleeding associated with a stringent anticoagulation regimen further increase the morbidity of the stenting procedure. The reported incidence of access site complications requiring vascular repair is 4% to 10%. The combined rate of vascular complications and bleeding complications at the access site or other sites that require transfusions varies considerably, from 7% to 20%. In the present study, stent insertion was performed for a variety of indications but was frequently performed electively. Lesion anatomy was complex in this cohort, as reflected by the 16% of lesions >15 mm, the 14% of tandem lesions, the 26% of lesions that were stented in angiographically small vessels (<3 mm), the high percentage of complex lesion morphology (modified AHA/ACC lesion types B2 or C), and the 3% of lesions with large filling defects consistent with thrombus. Despite the high complexity in this nonselected cohort of patients, the overall clinical success and complication rates compare favorably with those reported for elective or single stent deployment and those reported for the indications of acute or threatened closure.

As with prior studies, intravascular ultrasound was important in assessing adequate stent expansion, which was frequently underestimated by angiography. The most frequent site of potential flow limitation was within the stented segment. After intravascular ultrasound-guided repeat dilations, the intrastent lumen CSA was significantly enlarged, from 6.5 to 8.8 mm², P<.0001. With this approach, stent thrombosis was rare despite the absence of anticoagulation.

The primary focus of the present study was a short-term assessment of the safety of stent implantation without subsequent anticoagulation after intravascular ultrasound confirmation. The novelty of the approach that combines both improved stent expansion and the use of multiple stents for full lesion coverage also warranted a long-term assessment of outcome. Despite the complexity of the patients in this cohort, the 6-month event rate is only slightly higher than the event rates reported in multicenter trials on single stent implantation. The procedural complications in the early experience and the inclusions of patients with low ejection fraction contribute to the cumulative high death rate reported at 6 months.

Intravascular Ultrasound–Guided Stenting

By study design, intravascular ultrasound imaging was first performed after an initially successful angiographic result with <20% residual stenosis by visual analysis was obtained. Despite the angiographic appearance, measurements at the initial intravascular ultrasound study suggested that further dilatation was necessary in the majority of cases. The diameter and CSA of the stent lumen were enlarged significantly after repeat dilatation. Analysis of the intravascular ultrasound data provided other important information in evaluating the effect of various balloon dilatation strategies. The intravascular ultrasound data illustrated the overdilatation effect from the oversized balloon strategy. Balloons that were sized to the intravascular ultrasound vessel diameter (angiographically oversized) were used for final balloon dilations in the majority of the stent implantation procedures. This strategy was initially used to maximize protection against stent thrombosis in a large, unselected, and consecutive series of patients who were undergoing stent implantation without subsequent anticoagulation for the first time. Although protective against stent thrombosis, this strategy came with the price of a high procedural complication rate and an unacceptable incidence of intracoronary vessel rupture. The experience gained from intravascular ultrasound imaging together with an evaluation of clinical results affected the choice of balloon size and inflation pressures. As the study progressed, balloons selected on the basis of angiographic vessel size and higher pressures were used to provide adequate expansion within the stented segment. With the adjustment in the balloon dilatation strategy, the final stent expansion was more appropriate relative to the reference vessel measurements. This resulted in a lower intraprocedural complication rate but did not increase the incidence of stent thrombosis.

Full Lesion Coverage and Use of Multiple Stents

Intravascular ultrasound identified lesions in the adjacent unstented segments that were poorly visualized on angiogram. Typically, the angiogram at the corresponding site would reveal an area of ill-defined haziness without stenosis, a discrete stenosis <20% and less commonly, no evidence of a lesion. The decision to treat the lesions at the stent margins based on a quantitative assessment of their severity by intravascular ultrasound was in keeping with a practice of covering the full extent of the lesion. Both intravascular ultrasound and pathologic reports have shown that angiography underestimates the severity of coronary disease. In some instances, intravascular ultrasound imaging was also valuable in assisting in the decision not to deploy stents to lesions at the stent margins. The lesions that were stented tended to be in angiographically small vessels in which the lesions were more likely to encroach on the intravascular ultrasound catheter and in which the risk for stent thrombosis was perceived to be higher. In the majority of these lesions, the lumen CSA was <5 mm².

Previous stent investigations have identified residual lesions and dissections after stent implantation as a major cause of subsequent early...
Residual lesions (or dissections) after stent implantation are due either to a failure to cover the distal extent of a lesion or to the balloon dilatation process after successful stent deployment to the appropriate lesion site. In the present study, the use of more than one stent, when necessary, to achieve full lesion coverage may also be an important reason for the low incidence of stent thrombosis. The low incidence of stent thrombosis also demonstrates that the use of multiple stents for full lesion coverage is a safe strategy to use despite the lack of anticoagulation after the stent procedure.

Angiographic Versus Ultrasound Assessment

Well-defined angiographic criteria for successful stent expansion that alleviates the risk of stent thrombosis and the need for anticoagulation have not been developed. There is a limit to visual interpretation of small percent stenosis differences on the angiogram. It is arguable that careful on-line quantitative angiographic measurements could better determine angiographic success similar to the results achieved with intravascular ultrasound. The experience of this study showed that indentations in the balloon profile or angiographic mismatch between the measured and chosen balloon diameters correspond to inadequate stent expansion as documented by intravascular ultrasound. Empirical high-pressure balloon inflations with an appropriate-size noncompliant balloon may increase the number of patients who will have acceptable stent expansion. In the present study, high-pressure balloon inflations increased the percentage of patients who achieved adequate stent expansion at the initial intravascular ultrasound evaluation from 12% to 60%. Despite this aggressive inflation approach, 40% of the stents with an acceptable angiographic result still required additional dilatation with higher pressures or, less commonly, a dilatation with a larger balloon. The angiographic method of determining stent expansion has inherent limitations of a one-dimensional assessment of percent diameter stenosis. In contrast, intravascular ultrasound cross-sectional imaging from within the lumen of the stent is a reliable method of confirming adequate stent expansion with a degree of security that allows anticoagulation to be eliminated from the poststent medical regimen.

Antiplatelet Therapy

In this study, the majority of patients were treated with ticlopidine after stent insertion. In this group, there were two stent thrombosis events (0.8%). In the group treated with aspirin, there was one stent thrombosis event (1.4%) (P=NS). The two late stent occlusions occurred with the patients on aspirin (started after 1 to 2 months of ticlopidine therapy). The lack of difference in the stent thrombosis rates suggests that the achievement of adequate stent expansion and good flow in adjacent segments is a more important variable in the prevention of stent thrombosis than the specific antiplatelet agent. A randomized comparison may better determine whether small differences in efficacy exist between the two antiplatelet agents.

Study Limitations

One limitation was the absence of computerized quantitative coronary angiographic analysis. Another important methodological weakness was the lack of a consistent intravascular ultrasound criterion and balloon dilatation strategy. The change in the quantitative intravascular ultrasound criterion was based on knowledge gained during the course of the investigation and reflects an adjustment to a simplified criterion that is easier to achieve and may have more physiological meaning in terms of the prevention of stent thrombosis. After the initial experience showed a low stent thrombosis rate, balloon dilatation strategies were adapted in an attempt to reduce intra-procedural complications, which were unacceptably high. The evolving balloon dilatation strategy, however, significantly decreases the sample size for each phase and creates difficulties in discerning differences for low event rate complications such as stent thrombosis and coronary vessel rupture. Postprocedure complications associated with pre-stent rotational atherectomy contributed to two of the early postprocedural events. Although the Rotablator has utility in the treatment of lesions that resist dilatation, cautious use of this device may be warranted in the patient in whom stent implantation is anticipated. Short-term heparin for 24 hours may also be appropriate in this select situation.

One drawback to the technique of using intravascular ultrasound to assess the adequacy of stent expansion and lesion coverage is the increased number of stents and balloons and a longer procedure time. A more accurate analysis of the overall cost of the technique, however, should weigh the expense of increased procedural resources together with an evaluation of the savings from a decrease in postprocedural complications, a reduction in hospital stay, and the elimination of laboratory costs associated with monitoring anticoagulation regimens. The use of balloon delivery systems that incorporate a high-pressure balloon for the initial stent deployment would further reduce procedural costs and might also decrease dissections at stent margins that are due to balloon misplacement when stents are not visible.

The results of the study apply primarily to patients undergoing elective stent implantation, since the majority of patients underwent stent insertion for nonemergent indications. It is encouraging, however, that there were no stent thromboses in 21 consecutive patients who underwent emergency Palmaz-Schatz stent implantation despite not having postprocedural anticoagulation. Whether there is an absolute requirement of intravascular ultrasound to confirm stent expansion before treatment only with antiplatelet therapy was not addressed in the present investigation. A randomized, multicenter trial would perhaps best answer this issue in view of the important clinical and economic ramifications.

Conclusions and Future Directions

On the basis of these observations, it is reasonable to conclude that the Palmaz-Schatz stent can be deployed in coronary arteries with a low rate of thrombosis provided that stent expansion is adequate and there are no other flow-limiting lesions present. If high-pressure stent dilatation, treatment of the entire lesion, and intravascular ultrasound documentation of optimal stent expansion and lesion coverage are used, anticoagulation can be safely omitted after the procedure. This strategy should facilitate the expanded use of stents to provide the benefit of decreased restenosis while simultaneously reducing the cost and complications associated with stent insertion.

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