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A RANDOMIZED COMPARISON OF CORONARY-STENT PLACEMENT AND BALLOON ANGIOPLASTY IN THE TREATMENT OF CORONARY ARTERY DISEASE

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Abstract *Background.* Coronary-stent placement is a new technique in which a balloon-expandable, stainless-steel, slotted tube is implanted at the site of a coronary stenosis. The purpose of this study was to compare the effects of stent placement and standard balloon angioplasty on angiographically detected restenosis and clinical outcomes.

Methods. We randomly assigned 410 patients with symptomatic coronary disease to elective placement of a Palmaz–Schatz stent or to standard balloon angioplasty. Coronary angiography was performed at base line, immediately after the procedure, and six months later.

Results. The patients who underwent stenting had a higher rate of procedural success than those who underwent standard balloon angioplasty (96.1 percent vs. 89.6 percent, P = 0.011), a larger immediate increase in the diameter of the lumen (1.72±0.46 vs. 1.23±0.48 mm, P<0.001), and a larger luminal diameter immediately after the procedure (2.49±0.43 vs. 1.99±0.47 mm, P<0.001). At six months, the patients with stented lesions continued to have a larger luminal diameter (1.74±0.60 vs. 1.56±0.65 mm, P = 0.007) and a lower rate of restenosis (31.6 percent vs. 42.1 percent, P = 0.046) than those treated with balloon angioplasty. There were no coronary events (death; myocardial infarction; coronary-artery bypass surgery; vessel closure, including stent thrombosis; or repeated angioplasty) in 80.5 percent of the patients in the stent group and 76.2 percent of those in the angioplasty group (P = 0.16). Revascularization of the original target lesion because of recurrent myocardial ischemia was performed less frequently in the stent group than in the angioplasty group (10.2 percent vs. 15.4 percent, P = 0.06).

Conclusions. In selected patients, placement of an intracoronary stent, as compared with balloon angioplasty, results in an improved rate of procedural success, a lower rate of angiographically detected restenosis, a similar rate of clinical events after six months, and a less frequent need for revascularization of the original coronary lesion. (N Engl J Med 1994;331:496-501.)

THE long-term benefit of coronary balloon angioplasty is limited by the possibility of restenosis of the treated segment, which occurs in approximately 30 to 50 percent of patients.[1-4] Restenosis can be caused by several factors, including elastic recoil of the dilated artery, platelet-mediated thrombus formation, proliferation of smooth-muscle cells, and vascular remodeling.[5] When restenosis develops, it is frequently associated with recurrent myocardial ischemia that necessitates additional revascularization procedures. New approaches to coronary intervention have therefore been developed with the aim of reducing the possibility of restenosis. Debulking coronary atheroma with lasers or atherectomy has not improved the problem of restenosis.[6-9] However, preliminary evidence suggests that stents may reduce the chance of restenosis by decreasing the elastic recoil of the vessel and sealing intimal flaps, thus providing a wider, smoother coronary lumen.[10,11] To test this hypothesis, we conducted a prospective, randomized trial to compare the rates of restenosis with coronary-stent placement and standard balloon angioplasty.

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*Additional participants in the Stent Restenosis Study (STRESS) trial are listed in the Appendix.

METHODS

Participating Centers and Investigators

The study centers and investigators were selected on the basis of their experience with implantation of Palmaz–Schatz coronary stents. The study protocol was approved by the institutional review board at each of the 20 centers participating in the trial.

Patient Selection

The study population consisted of patients with symptomatic ischemic heart disease and new lesions of the native coronary circulation. The specific angiographic criteria for enrollment included at least 70 percent stenosis, according to the estimate of the investigators; a lesion that was 15 mm or less in length and could be spanned by a single stent; and a vessel diameter of at least 3.0 mm. The criteria for exclusion were a myocardial infarction within the previous seven days; a contraindication to aspirin, dipyridamole, or warfarin sodium; and a left ventricular ejection fraction of 40 percent or less. The angiographic criteria for exclusion were evidence of coronary thrombus, the presence of multiple focal lesions or diffuse disease, serious disease in the left main coronary artery, ostial lesions, and severe vessel tortuosity.

Randomization

After the patients had been interviewed to determine their eligibility and had given their informed consent, they were randomly

assigned to either stent placement or balloon angioplasty. Randomization of the patients, stratified according to center with a block design, was carried out by means of sealed envelopes. The randomization sequence was developed so that an equal number of patients would be assigned to each treatment at each center.

Procedural Protocol

Stent Placement

The Palmaz–Schatz stent is composed of two rigid 7-mm slotted stainless-steel tubes connected by a 1-mm central bridging strut (Johnson and Johnson Interventional Systems, Warren, N.J.). The stent, which is 1.6 mm in diameter in the unexpanded state, is mounted on a balloon catheter and protected by an outer sheath during passage to the target site. When the sheath is withdrawn, inflation of the balloon catheter expands the stent. Technical details of the design and placement of the Palmaz–Schatz coronary stent have been described elsewhere.[12,13]

Patients assigned to stent placement received nonenteric aspirin (325 mg daily), dipyridamole (75 mg three times a day), and treatment with a calcium-channel antagonist, initiated at least 24 hours before the procedure. In addition, patients received intravenous low-molecular-weight dextran (dextran 40, given at a dose of 100 ml per hour for two hours before stenting and at a dose of 50 ml per hour during and after the procedure, for a total volume of 1 liter). During the procedure, patients received an initial bolus injection of heparin (10,000 to 15,000 units) supplemented as needed to maintain an activated clotting time of more than 300 seconds. The heparin infusion was discontinued at the termination of the procedure and reinstituted four to six hours after hemostasis of the site of vascular access had been achieved. Warfarin sodium was begun on the day of the procedure. Heparin and warfarin sodium were both administered for at least 72 hours or until a prothrombin time of 16 to 18 seconds had been achieved (international normalized ratio, 2.0 to 3.5). After patients were discharged from the hospital, dipyridamole and warfarin sodium were continued for one month, and aspirin was continued indefinitely.

Angioplasty Protocol

Angioplasty was performed with the use of conventional techniques. Aspirin was prescribed, but warfarin sodium was not administered. Investigators attempted to achieve an optimal result with balloon angioplasty, which was defined as residual stenosis of less than 30 percent of the luminal diameter, according to a visual estimate. A crossover to stent placement was permitted as a "bail-out" procedure in the case of abrupt or threatened closure, defined as a dissection of the artery with compromised antegrade blood flow (Thrombolysis in Myocardial Infarction [TIMI] grade, <3) or persistent stenosis of over 50 percent of the luminal diameter in association with evidence of myocardial ischemia (chest pain, electrocardiographic changes, or both).

Follow-up

Patients were required to have clinical follow-up studies after one, three, and six months. Coronary angiography was required at six months in all the patients except those who had died or undergone coronary-artery bypass surgery or repeated angioplasty for abrupt closure during the first 14 days after the initial revascularization. Angiography performed before four months was allowed on the basis of clinical indications. However, if restenosis was not found, a subsequent angiogram was obtained after four months.

Angiographic Analysis

Angiography was performed in two orthogonal views. Intracoronary nitroglycerin (200 mg) was injected before all angiographic assessments. Angiograms were analyzed at the Core Angiographic Laboratory at Jefferson Medical College. Quantitative analysis was performed with the use of a validated edge-detection algorithm.[14] Vessel edges were determined with the computerized algorithm, and luminal diameters were measured with the dye-filled catheter as a reference. The diameters of the normal segments proximal and distal to the treated area were averaged to determine the reference diameter. The minimal luminal diameter, reference diameter, and percentage of stenosis were calculated as the mean values from two orthogonal projections. The percentage of elastic recoil was defined as the largest inflated-balloon diameter minus the postprocedural minimal luminal diameter divided by the inflated-balloon diameter. In addition, coronary lesions were assessed for eccentricity, calcification, thrombus, plaque ulceration, tortuosity, and postprocedural dissection. Definitions used for this morphologic analysis and prior validation studies of the quantitative angiographic analysis have been described elsewhere.[11,13,15]

End Points

The primary end point of the trial was angiographic evidence of restenosis, defined as at least 50 percent stenosis on the follow-up angiogram. Secondary angiographic end points included angiographic evidence of procedural success and the absolute minimal luminal diameter after the procedure and at follow-up. Angiographic evidence of procedural success was defined as a reduction in stenosis to 50 percent or less by quantitative analysis.

Clinical evidence of procedural success was defined as angiographic evidence of success without a major complication (death, myocardial infarction, or coronary-artery bypass surgery) during the index hospitalization. The secondary clinical end point was a composite end point, defined as whichever of the following occurred first: death, myocardial infarction, coronary bypass surgery, or the need for repeated angioplasty within the first 6 months (±60 days) after the initial revascularization. Myocardial infarction was documented by the presence of new Q waves of at least 0.04 second's duration or a creatine kinase level or MB fraction at least twice the upper limit of normal. Clinical events were classified as early (occurring from day 0 to day 14) or late (occurring after 14 days). Revascularization of the target lesion was defined as angioplasty or bypass surgery performed because of restenosis of the target lesion in association with recurrent angina, objective evidence of myocardial ischemia, or both. Other events included abrupt vessel closure (after the patient had left the catheterization laboratory) and hemorrhagic complications, defined as a cerebrovascular accident, bleeding requiring transfusion, or the need for vascular surgery.

Clinical and angiographic data were forwarded to the Data Coordinating Center at the University of Pittsburgh for statistical analyses. Adverse events were audited and reviewed by members of the Steering Committee. The primary analysis of angiographic and procedural outcomes was based on the intention-to-treat principle. We also performed a secondary analysis of the rate of restenosis according to the treatment received.

For the analysis of continuous data, two-tailed t-tests were used to assess differences between the two treatment groups. The results are expressed as means ±SD. Categorical data, which are presented as rates, were compared by chi-square test, except for the composite clinical end point and revascularization of the target lesion, which were analyzed by means of Kaplan–Meier survival curves, with differences between the two treatment groups compared by Wilcoxon test.[16] Multiple linear regression was used to assess the relation between the luminal diameter at follow-up and multiple clinical and angiographic variables, including age, sex, location of the lesion, vessel diameter, and postprocedural luminal diameter.

Results

Between January 1991 and February 1993, 410 patients were enrolled in the study; 207 patients were randomly assigned to stent placement, and 203 to angioplasty. After randomization, three patients (two in the stent group and one in the angioplasty group) were excluded because they did not meet all the enrollment criteria. Thus, the final study group comprised 407 patients. Their base-line clinical and angiographic characteristics are shown in Table 1. More

men were assigned to the stent group than to the angioplasty group, and the patients in the stent group had lesions that were slightly longer, with a higher incidence of eccentricity, but the two groups were well matched with respect to other clinical characteristics.

Procedural and Early Clinical Outcome

Stents were placed in 197 of the 205 patients (96.1 percent) randomly assigned to this therapy. One patient, in whom stent placement failed because of an inability to cross the lesion with a guide wire, was treated medically. Seven patients were switched to angioplasty: three because of an inability to place the stent and four because of lesion characteristics deemed unfavorable for stent placement at the time of the procedure. In the angioplasty group, six patients required emergency coronary-artery bypass surgery. In addition, 15 patients were switched to alternative therapies: 14 (6.9 percent) to emergency stent placement as a bailout procedure (1 of the 14 subsequently required emergency bypass surgery) and 1 to directional atherectomy.

Table 1. Base-Line Clinical and Angiographic Characteristics of Patients Assigned to Stent Placement or Angioplasty.*

Characteristic	Stent Group (N = 205)	Angioplasty Group (N = 202)
Male — % of patients	83	73†
Age — yr	60±10	60±10
Diabetes — % of patients	15	16
Hypertension — % of patients	43	45
Hyperlipidemia — % of patients	44	48
Current smoker — % of patients	21	24
History of myocardial infarction — % of patients	37	36
Recent myocardial infarction (within previous 6 wk) — % of patients	18	15
Unstable angina — % of patients	47	48
Pain at rest	33	39
Pain with electrocardiographic changes	23	26
Postinfarction angina	7	6
No. of diseased vessels — % of patients		
1	64	68
2	27	21
3	9	11
Ejection fraction — %	61±12	61±11
Target vessel — % of patients		
Left anterior descending	47	48
Left circumflex	16	13
Right coronary artery	37	39
Calcification — % of patients	17	15
Thrombus — % of patients		
Definite	2	1
Possible	15	9
Eccentricity — % of patients	66	54‡
Lesion angulation >45° — % of patients	13	18
Lesion length — mm	9.6±3.0	8.7±2.7§
Stenosis — % of luminal diameter	75±9	75±8

*Plus–minus values are means ±SD.
†P≤0.05.
‡P = 0.02.
§P<0.001.

Table 2. Procedural Outcomes and Clinical Events.

Variable	Stent Group (N = 205)	Angioplasty Group (N = 202)	P Value
	% of patients		
Procedural outcome			
Angiographic success			
Reading at study center	99.5	96.5	0.04
Quantitative analysis	99.5	92.6	<0.001
Clinical success	96.1	89.6	0.011
Early events (0–14 days)			
Death	0	1.5	0.12
Myocardial infarction/Q wave	5.4/2.9	5.0/3.0	0.85/1.0
Coronary bypass surgery	2.4	4.0	0.38
Abrupt closure*	3.4	1.5	0.34
Repeated angioplasty	2.0	1.0	0.69
Any event	5.9	7.9	0.41
Late events (15–240 days)			
Death	1.5	0	0.25
Myocardial infarction/Q wave	1.5/1.0	2.0/0.5	0.72/1.0
Coronary bypass surgery	2.4	4.5	0.26
Repeated angioplasty	9.8	11.4	0.59
Target-vessel revascularization	10.2	15.4	0.06
Any event	15.1	15.8	0.84
All events (0–240 days)			
Death	1.5	1.5	0.99
Myocardial infarction/Q wave	6.3/3.4	6.9/3.5	0.81/0.98
Coronary bypass surgery	4.9	8.4	0.15
Repeated angioplasty	11.2	12.4	0.72
Any event	19.5	23.8	0.16
Bleeding and vascular complications			
Cerebrovascular accident	1.0	0.5	1.0
Surgical vascular repair	3.9	2.0	0.25
Bleeding requiring transfusion	4.9	2.5	0.11
Any event	7.3	4.0	0.14

*After the patient left the catheterization laboratory.

Procedural and early clinical outcomes are shown in Table 2. According to the quantitative analysis, there was angiographic evidence of procedural success in 204 of the 205 patients (99.5 percent) randomly assigned to undergo stent placement and in 187 of the 202 patients (92.6 percent) randomly assigned to undergo angioplasty (P<0.001). The clinical success rates were 96.1 percent and 89.6 percent, respectively (P = 0.011).

Abrupt vessel closure occurred in 10 patients after they had left the catheterization laboratory: 7 in the stent group and 3 in the angioplasty group (3.4 and 1.5 percent, respectively; P = 0.34). In the three patients in the angioplasty group, the closure occurred after the stent had been placed as a bailout measure. Abrupt closure occurred an average of 6 days (range, 2 to 14) after the procedure, and in 6 of the 10 patients, it occurred after hospital discharge. All the patients with abrupt closures had major cardiac events (two died and eight had nonfatal myocardial infarctions). The proportions of patients with any major cardiac event (death, myocardial infarction, coronary bypass surgery, or repeated angioplasty within 14 days after the procedure) were 5.9 percent in the stent group and 7.9 percent in the angioplasty group

(Table 2). Bleeding and vascular complications occurred more commonly in the stent group than in the angioplasty group (7.3 percent vs. 4.0 percent, P = 0.14). The hospital stay after the procedure was longer in the stent group (5.8 days vs. 2.8 days, P<0.001).

Angiographic Results

Angiography was repeated at six months in 336 of the 383 patients (88 percent) eligible for follow-up. Angiography was not repeated in 28 patients in the stent group because of refusal (15 patients) or ineligibility due to stent thrombosis (7), death (3), early coronary bypass surgery (2), or inability to perform the study procedures (1). In the angioplasty group, 43 patients did not have follow-up angiography because of refusal (32) or ineligibility due to early coronary bypass surgery (7), abrupt vessel closure (3), or death (1). The rate of restenosis was 31.6 percent (56 of 177 patients) in the stent group and 42.1 percent (67 of 159) in the angioplasty group (P = 0.046). The rates of restenosis among the patients who received their assigned therapy were 30.0 percent in the stent group and 43.0 percent in the angioplasty group (P = 0.016).

The luminal dimensions at base line, immediately after the procedure, and at follow-up are shown in Table 3. At base line, there was no difference in the reference diameter or the severity of stenosis between the two groups. After the procedure, a larger immediate gain in the luminal diameter was achieved in the patients who underwent stent placement than in those who underwent angioplasty, resulting in a larger mean (±SD) diameter in the stent group (2.49±0.43 vs. 1.99±0.47 mm, P<0.001). At follow-up, the stent group had a larger mean reduction in the luminal diameter (0.74±0.58 vs. 0.38±0.66 mm, P<0.001) but a larger net gain, resulting in a larger luminal diameter at follow-up (1.74±0.60 vs. 1.56±0.65 mm, P = 0.007). These data are shown in Figure 1. A stepwise linear regression analysis showed that the luminal diameter immediately after the procedure was the most important predictor of the luminal diameter at six months (b = 0.41, P<0.001), irrespective of the procedure used. Additional important determinants included a larger reference diameter (b = 0.31, P<0.001) and location of the lesion in a vessel other than the left anterior descending coronary artery (b = 0.14, P = 0.029).

Late Clinical Follow-up

Data on late cardiac events and all events are shown in Table 2. Clinical follow-up data were available for 406 of the 407 patients. Although the numbers of patients who died or had myocardial infarctions were comparable in the two groups, fewer patients in the stent group underwent revascularization of the target lesion (10.2 percent vs. 15.4 percent, P = 0.06) (Fig. 2). Event-free survival was 80.5 percent in the stent group, as compared with 76.2 percent in the angioplasty group (P = 0.16) (Fig. 3). Among the patients eligible for follow-up, a larger proportion of those in the stent group remained free of angina (78.9 percent vs. 71.1 percent, P = 0.076).

Table 3. Angiographic Results in the Stent and Angioplasty Groups.*

Variable	Stent Group (N = 205)	Angioplasty Group (N = 202)	P Value
Before the procedure			
Reference vessel (mm)	3.03±0.42	2.99±0.50	0.30
Minimal luminal diameter (mm)	0.77±0.27	0.75±0.25	0.48
Stenosis (% of luminal diameter)	75±9	75±8	0.81
After the procedure			
Reference vessel (mm)	3.05±0.40	2.99±0.46	0.15
Minimal luminal diameter (mm)	2.49±0.43	1.99±0.47	<0.001
Stenosis (% of luminal diameter)	19±11	35±14	<0.001
Elastic recoil (%)	15±11	24±15	<0.001
Dissection (% of patients)	7	25	<0.001
At follow-up			
Reference vessel (mm)	3.00±0.41	2.98±0.49	0.74
Minimal luminal diameter (mm)	1.74±0.60	1.56±0.65	0.007
Stenosis (% of luminal diameter)	42±18	49±19	0.001
Restenosis (% of patients)	31.6	42.1	0.046
Change in minimal luminal diameter			
Immediate gain (mm)	1.72±0.46	1.23±0.48	<0.001
Late loss (mm)	0.74±0.58	0.38±0.66	<0.001
Net gain (mm)	0.98±0.62	0.80±0.63	0.01

*Plus–minus values are means ±SD. Immediate gain refers to the minimal luminal diameter immediately after the procedure minus the diameter before the procedure. Late loss refers to the minimal luminal diameter immediately after the procedure minus the diameter at follow-up. Net gain refers to the minimal luminal diameter at follow-up minus the diameter before the procedure.

Discussion

In this trial, we compared stent placement with balloon angioplasty for the treatment of new focal coronary stenoses in larger vessels; we found a reduc-

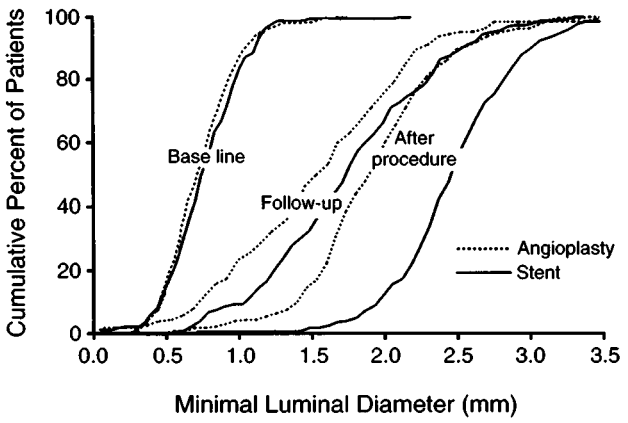

Figure 1. Minimal Diameter of the Lumen at Base Line, Immediately after Stent Placement or Angioplasty, and at Follow-up.

There was no difference in base-line values between the stent and angioplasty groups. Immediately after the procedure, the patients in the stent group had a larger minimal luminal diameter than those in the angioplasty group. Six months later, both groups had reduced values, and a significant difference in diameter persisted between the two groups.

tion in the rate of angiographic restenosis at six months with the stenting procedure. This reduction was associated with a reduction in the need for repeat revascularization due to ischemia-associated restenosis.

Our findings contrast with those of previous investigations that examined the efficacy of pharmacologic agents in preventing restenosis.[17-24] Of the newer interventional procedures, only directional atherectomy has been subjected to careful prospective, randomized studies to assess its efficacy in reducing restenosis, as compared with the efficacy of angioplasty.[7,8] Those studies showed either no benefit of atherectomy or a minimal reduction in restenosis with more frequent major complications.

Like the Coronary Angioplasty versus Excisional Atherectomy Trial (CAVEAT),[7] our study shows that the most important determinant of the luminal diameter at six months was the luminal diameter achieved immediately after the procedure. It seems plausible that the reduction in restenosis in our stent group was due to the significantly larger luminal diameter obtained immediately after placement of the stent, as compared with the luminal diameter immediately after angioplasty. The residual stenosis in the stent group (19 percent) was roughly half that in the angioplasty group (35 percent) and 10 percentage points less than the residual stenosis in patients undergoing directional atherectomy.[7] Although the larger immediate gain in luminal diameter was offset by a larger subsequent loss, the net gain remained larger in the patients in the stent group (Fig. 1). Multivariate analysis showed that the luminal diameter immediately after the procedure was the most powerful predictor of the luminal diameter at follow-up, regardless of whether stenting or balloon angioplasty achieved this result. Therefore, it was not the specific technique used, but rather its efficacy in achieving a larger luminal diameter that was the determining factor, an idea that has been suggested previously.[25] In addition, stenting resulted in a larger diameter with less risk of intimal disruption and elastic recoil, thereby acting as an effective intravascular scaffold. The ability of the stent to serve as a scaffold was further demonstrated in the 14 patients in the angioplasty group (6.9 percent) who were switched to stent placement for treatment of imminent or actual closure after balloon angioplasty had failed. At the inception of this trial, stent placement as a bailout measure, which at the time was not available as a routine procedure, was considered equivalent to emergency coronary-artery bypass surgery. Thirteen of the 14 patients who underwent stent placement as a bailout measure had balloon-induced dissections or luminal compromise associated with chest pain or electrocardiographic changes, suggesting that these patients would have had serious clinical events if stent placement had not been available. Therefore, the availability of stent placement probably decreased the rate of clinical events in the angioplasty group. This study thus represents a comparison of two treatment strategies: elective stent placement and elective balloon angioplasty with stent placement available as a bailout measure.

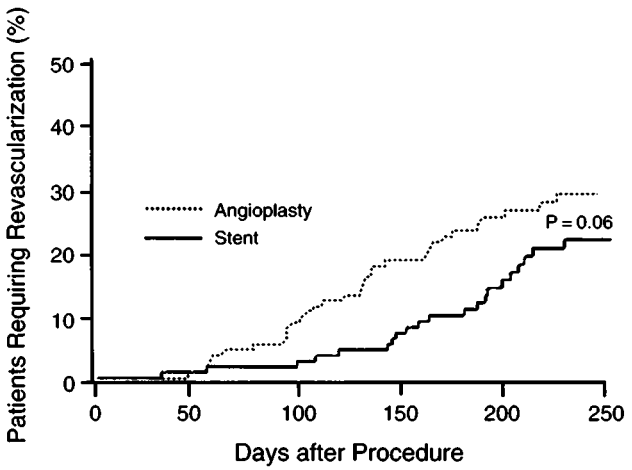

Figure 2. Kaplan–Meier Curves for Revascularization of the Target Lesion.

Fewer patients in the stent group than in the angioplasty group required revascularization of the target lesion because of ischemia.

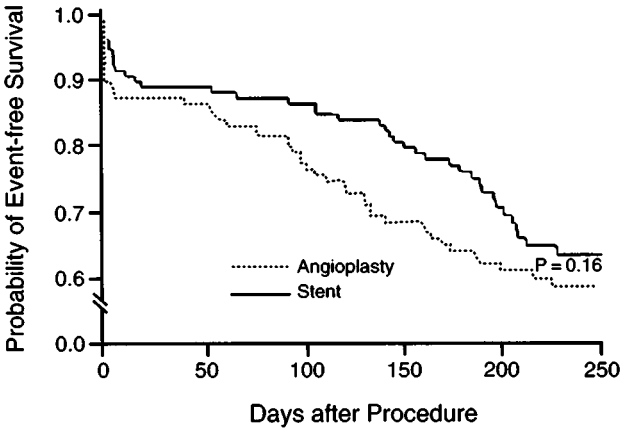

Figure 3. Kaplan–Meier Survival Curves for Major Cardiac Events (Death, Myocardial Infarction, Coronary-Artery Bypass Surgery, and Repeated Angioplasty).

Several limitations of stent placement need to be emphasized. Stent thrombosis occurred in 3.4 percent of the patients who underwent stent placement as an elective procedure and in 21.4 percent of those in whom stent placement was used as a bailout technique. These thrombotic events occurred 2 to 14 days after placement of the stent, with six instances of thrombosis after discharge, and invariably resulted in major clinical complications. Furthermore, the intense anticoagulation and antiplatelet regimen associated with stent placement resulted in nearly twice the number of hemorrhagic and peripheral vascular complications associated with angioplasty, as well as a prolonged hospital stay.

Although the frequency with which follow-up angiography was performed was relatively high in both

groups, there was a higher rate of angiographic follow-up in the stent group (92 percent vs. 83 percent, $P = 0.008$). This difference, which may bias the rate of restenosis in favor of stent placement, is a limitation of the study.

In conclusion, elective stent placement, as compared with angioplasty, has a higher clinical success rate and reduces the incidence of restenosis and the need for subsequent revascularization of the treated lesion. The reduction in restenosis is not associated with an increase in major cardiac events, despite the limitations imposed by stent thrombosis and hemorrhagic complications. The use of antithrombotic stent coatings, improved techniques to optimize expansion of the stent during implantation, and compression and closure devices at the site of arteriotomy may address these limitations. If they are effectively overcome, implantation of the Palmaz–Schatz stent may become the preferred treatment in selected patients with new lesions in large coronary arteries.

Appendix

The following institutions and investigators participated in the STRESS trial: Arizona Heart Institute, Phoenix (E. Davis, W. Catran, and K. Waters); Beth Israel Hospital, Boston (D.J. Diver, J. Carrozza, and C. Senerchia); Centro Cuore Columbus, Milan, Italy (Y. Almagor and M. Bernati); Cleveland Clinic Foundation, Cleveland (P. Whitlow); Florida Heart Hospital, Orlando (C. Curry, C.B. Saenz, W.H. Willis, Jr., R.J. Ivanhoe, and N. Granger); Hospital of the University of Pennsylvania, Philadelphia (H. Herman, D. Kolansky, W. Laskey, and D. DiAngelo); Johns Hopkins Hospital, Baltimore (V. Coombs); Lenox Hill Hospital, New York (E.M. Kreps, J. Strain, N. Cohen, J. Higgins, and C. Undemir); Scripps Clinic and Research Foundation, San Diego, Calif. (N. Morris and M. Dowling); St. Luke's Hospital, Houston (M. Harlan and B. Lambert); Thomas Jefferson University Hospital, Philadelphia (A. Zalewski, P. Walinsky, and D. Porter); Toronto General Hospital, Toronto (L. Lazzam, C. Lazzam, and P. Slaughter); University of Texas at San Antonio, San Antonio (J.P. Hennecken, S. Kiesz, and A. Briscoe); Vancouver General Hospital, Vancouver, B.C. (C.E. Buller and A. McCarthy); Victoria General Hospital, Halifax, N.S. (B. O'Neil, C.J. Foster, C.M. Peck, K.A. Foshay, and N.L. Fitzgerald); Victoria Hospital, London, Ont. (N. Murray-Parson and L. Marziali); Washington Cardiology Center, Washington, D.C. (K. Donovan); Yale University, New Haven, Conn. (H.S. Cabin and R.E. Rosen); *Data Coordinating Center:* Department of Epidemiology, University of Pittsburgh, Pittsburgh (K. Detre, V. Niedermeyer, L. Kennard, and L. Vetri); *Core Angiographic Laboratory:* Thomas Jefferson University Hospital, Philadelphia (R. Rake, S. Gebhardt, D.L. Fischman, M.P. Savage, and S. Goldberg); *Steering Committee:* D.S. Baim, S. Goldberg, M.B. Leon, I. Penn, and R.A. Schatz.

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