

CORONARY-ARTERY STENTING COMPARED WITH BALLOON ANGIOPLASTY FOR RESTENOSIS AFTER INITIAL BALLOON ANGIOPLASTY

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ABSTRACT

Background Intracoronary stenting reduces the rate of restenosis after angioplasty in patients with new coronary lesions. We conducted a prospective, randomized, multicenter study to determine whether intracoronary stenting, as compared with standard balloon angioplasty, reduces the recurrence of luminal narrowing in restenotic lesions.

Methods A total of 383 patients who had undergone at least one balloon angioplasty and who had clinical and angiographic evidence of restenosis after the procedure were randomly assigned to undergo standard balloon angioplasty (192 patients) or intracoronary stenting with a Palmaz-Schatz stent (191 patients). The primary end point was angiographic evidence of restenosis (defined as stenosis of more than 50 percent of the luminal diameter) at six months. The secondary end points were death, Q-wave myocardial infarction, bypass surgery, and revascularization of the target vessel.

Results The rate of restenosis was significantly higher in the angioplasty group than in the stent group (32 percent as compared with 18 percent, $P=0.03$). Revascularization of the target vessel at six months was required in 27 percent of the angioplasty group but in only 10 percent of the stent group ($P=0.001$). This difference resulted from a smaller mean (\pm SD) minimal luminal diameter in the angioplasty group (1.85 ± 0.56 mm) than in the stent group (2.04 ± 0.66 mm), with a mean difference of 0.19 mm ($P=0.01$) at follow-up. Subacute thrombosis occurred in 0.6 percent of the angioplasty group and in 3.9 percent of the stent group. The rate of event-free survival at 250 days was 72 percent in the angioplasty group and 84 percent in the stent group ($P=0.04$).

Conclusions Elective coronary stenting was effective in the treatment of restenosis after balloon angioplasty. Stenting resulted in a lower rate of recurrent stenosis despite a higher incidence of subacute thrombosis. (N Engl J Med 1998;339:1672-8.)

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AN important limitation of coronary balloon angioplasty is restenosis, which occurs in 30 to 50 percent of patients.¹⁻⁵ Independent risk factors for restenosis are a recent history of angina pectoris and a previous myocardial infarction.⁶⁻¹⁰ Structural risk factors, such as a large degree of luminal narrowing before angioplasty, a small diameter of the reference segment, a symmetric lesion, an extensive area of plaque, and residual stenosis, have been identified.¹¹⁻¹³ After adjust-

ment for other risk factors, such as diabetes mellitus and proximal lesions in the left anterior descending coronary artery, there is only a slight difference in the rate of restenosis between first and successive coronary angioplasties.^{12,14}

Treatment directed to the mechanism of restenosis is needed in order to prevent this problem.¹⁵ Coronary stenting has been found to be effective in preventing coronary dissections, impending occlusions, and acute elastic recoil.¹⁶⁻¹⁸ The restenosis rate is reduced after stent implantation for new coronary stenoses.^{19,20}

The purpose of this study was to determine whether coronary stenting, as compared with balloon angioplasty, reduces the frequency of restenosis after previously successful balloon angioplasty. We performed a multicenter, randomized trial to compare the rate of restenosis after coronary stent placement with the rate after standard balloon angioplasty in patients with a first or subsequent restenosis.

METHODS

Selection of Patients

The study group consisted of patients with symptomatic ischemic heart disease due to a single lesion in a coronary artery after a successful first, second, third, or subsequent balloon angioplasty, with a luminal renarrowing of more than 50 percent.²¹ The lesion had to be less than or equal to 10 mm in length, with evidence of a clinical effect (angina pectoris or an abnormal finding on stress electrocardiography or thallium-201 scanning). The study was carried out according to the principles of the Declaration of Helsinki. Oral or written informed consent was obtained from all patients according to local practice. The study was approved by an independent ethics committee in Freiburg, Germany.

Balloon Angioplasty and Stent Implantation

Angioplasty was performed in the conventional manner by the femoral approach, according to the standard technique used at the participating centers. Aspirin was prescribed, and 15,000 IU of heparin was given as a bolus during the procedure. A goal of less than 30 percent residual stenosis was set to obtain an optimal

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result of angioplasty. Crossover to stent implantation was allowed when a symptomatic dissection occurred that could not be managed by repeated, prolonged angioplasty with the use of conventional or perfusion balloons.

For stenting, the Palmaz-Schatz stent (Johnson and Johnson Interventional Systems, Warren, N.J.) was used after the angioplasty procedure. This stent consists of two 7-mm, slotted, stainless-steel parts connected by a 1-mm central bridge segment. The stent was protected by a sheath to permit its passage through the vessel to the culprit lesion without the risk of embolization. After removal of the sheath, the balloon was inflated with up to 10 atmospheres of pressure, and the stent was expanded. The operators were advised to use a larger balloon and higher pressure, if necessary, to achieve a balloon-to-vessel ratio of 1.1 to 1.2, as described previously.^{22,23}

After angioplasty, patients received 300 mg of aspirin. After stenting, intravenous heparin was also administered until full anticoagulation had been achieved with oral phenprocoumon at an international normalized ratio of 2.0 to 3.5 during hospitalization. Oral anticoagulant therapy was continued for three months in the stent group.

Angiographic Analysis

In patients assigned to balloon angioplasty alone, coronary angiograms were obtained before and after angioplasty and at six months. In patients assigned to coronary stenting, angiograms were obtained before and after balloon angioplasty, after stenting, and at six months, except in those who had recurrent symptoms requiring interventions sooner. All coronary angiograms were analyzed in the central laboratory at the University of Essen, Essen, Germany.

Quantitative coronary angiography was performed with the use of the edge-detection system developed by Reiber et al. (Cardiovascular Measurement System, Medis Medical Imaging Systems, Leiden, the Netherlands).²⁴ With this system, the mean variation in the absolute diameter is ≤ 0.13 mm.²⁴ For calibration, the non-contrast-filled guiding catheter was used. The vessel diameters proximal and distal to the lesion were used to interpolate the reference diameter. From two orthogonal views, the minimal diameter of the lumen, the interpolated reference diameter, and the percentage of stenosis were calculated as described elsewhere.¹⁸ In addition, the immediate gain, late loss, and net gain in the luminal diameter and the late-loss index were calculated.^{19,20} (The immediate gain is the diameter immediately after the procedure minus the reference diameter before the procedure, the late loss is the diameter immediately after the procedure minus the diameter at follow-up, the net gain is the diameter at follow-up minus the reference diameter before the procedure, and the late-loss index is the late loss divided by the reference diameter before the procedure.)

Study End Points

The primary end point of the trial was angiographic evidence of restenosis, defined as stenosis of more than 50 percent of the luminal diameter, at six months. Secondary end points, for an analysis of event-free survival, included death, myocardial infarction, bypass surgery, and revascularization of the target vessel after randomization.²¹ Patients who refused coronary angiography at six months were contacted by telephone; none reported major cardiac events.

Myocardial infarction was documented on the basis of the development of a new Q wave of more than 0.04 second, with an increase in the creatine kinase level to more than twice the normal value and an increase in the MB fraction to more than 6 percent of the total creatine kinase level; non-Q-wave infarction was documented only on the basis of cardiac-enzyme values. Revascularization of the target lesion was defined as angioplasty or bypass surgery because of recurrent angina pectoris or signs of ischemia. Stent thrombosis was defined as total or subtotal occlusion of the vessel, with visualization of filling defects, within 24 hours after stenting (acute) or after 24 hours (subacute). Other events recorded included bleeding in the groin, whether or not blood transfusion

was required, and gastrointestinal, retroperitoneal, and cerebrovascular bleeding.²¹

Statistical Analysis

Categorical data, which are presented as rates, were compared by the chi-square test or Fisher's exact test, except for the clinical end points of death, myocardial infarction, and revascularization of the target vessel, which were analyzed by means of Kaplan-Meier survival curves, with differences between the two treatment groups compared by the log-rank test.^{25,26} Two-sided P values are reported.

RESULTS

From October 1991 to May 1996, 383 patients at 18 centers were enrolled in the study and randomly assigned to angioplasty (192 patients) or stenting (191). Sixteen patients in the angioplasty group and 13 in the stent group had angiograms that could not be analyzed. Thus, 176 patients in the angioplasty group and 178 in the stent group had angiograms suitable for analysis. Follow-up coronary angiograms were available for 158 of the 176 patients in the angioplasty group (90 percent) and for 156 of the 178 patients in the stent group (88 percent). The mean (\pm SD) follow-up time was 5.9 ± 1.3 months. There were no significant differences in base-line characteristics between the two groups (Table 1).

Quantitative Coronary Angiography

At base line, the minimal luminal diameter of the target vessel and the reference diameter were similar in the two groups (Table 2). The minimal luminal diameter was slightly, but not significantly, smaller in the stent group (after dilation in preparation for stenting) than in the angioplasty group. In the stent group, implantation of the stent and additional dilation after implantation resulted in a mean (\pm SD) luminal diameter of 3.02 ± 0.43 mm, which was significantly larger than the final luminal diameter in the angioplasty group ($P=0.001$).

On the basis of the follow-up angiograms, the minimal luminal diameter was significantly smaller in the angioplasty group than in the stent group, with a mean difference of 0.19 mm (Fig. 1 and Table 2). On average, stent implantation resulted in a larger immediate gain and a larger late loss in the minimal luminal diameter. When the immediate gain and late loss were considered together, the net gain was significantly greater after stent implantation than after angioplasty. The rate of restenosis was 18 percent in the stent group and 32 percent in the angioplasty group ($P=0.03$).

Technical Success

In the angioplasty group 12 of the 176 patients (7 percent) had symptomatic dissection requiring bailout stenting (crossover); the rate of technical success in this group was 93.2 percent. In two patients in the stent group, the lesion could not be crossed with the stent; thus, the rate of technical success in this group was 98.9 percent ($P=0.01$).

TABLE 1. BASE-LINE CHARACTERISTICS OF PATIENTS ASSIGNED TO BALLOON ANGIOPLASTY OR STENT PLACEMENT, CHARACTERISTICS OF THE PROCEDURE, AND OUTCOME.*

| VARIABLE | ANGIOPLASTY GROUP (N=176) | STENT GROUP (N=178) |
|-------------------------------------------------|---------------------------|---------------------|
| Age — yr | 60±8 | 59±10 |
| Weight — kg | 78±12 | 77±12 |
| Height — cm | 172±9 | 170±8 |
| Male sex — no. (%) | 144 (82) | 142 (80) |
| Risk factors — no. (%) | | |
| Diabetes mellitus | 27 (15) | 36 (20) |
| Hypertension | 84 (48) | 81 (46) |
| Hyperlipidemia | 110 (62) | 87 (49) |
| Smoking | 102 (58) | 89 (50) |
| Clinical features — no. (%) | | |
| Unstable angina pectoris | 38 (22) | 30 (17) |
| Previous myocardial infarction | 73 (41) | 65 (37) |
| Previous bypass surgery | 5 (3) | 6 (3) |
| Previous angioplasty | 176 (100) | 178 (100) |
| First restenosis | 163 (93) | 168 (94) |
| Second restenosis | 10 (6) | 7 (4) |
| Third or subsequent restenosis | 3 (2) | 3 (2) |
| Vessel involvement — no. (%) | | |
| Single-vessel disease | 119 (68) | 120 (67) |
| Multivessel disease | 57 (32) | 58 (33) |
| Target artery | | |
| Left anterior descending | 101 (57) | 107 (60) |
| Left circumflex | 23 (13) | 22 (12) |
| Right coronary | 52 (30) | 49 (28) |
| Lesion type† | | |
| A | 58 (33) | 55 (31) |
| B1 | 62 (35) | 68 (38) |
| B2 | 44 (25) | 39 (22) |
| C | 12 (7) | 16 (9) |
| Calcification | 35 (20) | 38 (21) |
| Eccentricity | 62 (35) | 67 (38) |
| Procedural characteristics | | |
| Final balloon diameter — mm | 3.5±0.3 | 3.7±0.3 |
| Maximal inflation pressure — atm | 8±3 | 11±4 |
| Maximal inflation time — sec | 55±38 | 35±28 |
| High-pressure stent dilation (12 atm) — no. (%) | — | 48 (27) |
| Procedural outcome — no. (%) | | |
| Procedural success | 176 (100) | 178 (100) |
| Bailout stenting (crossover) | 12 (6.8) | — |
| Stent failure | — | 2 (1) |

*Plus-minus values are means ±SD. P<0.001 for all comparisons.

†The type of lesion was determined according to the American Heart Association–American College of Cardiology classification.

Clinical Events

The cumulative incidence of clinical events during hospitalization and after six months of follow-up in patients assigned to balloon angioplasty or stent placement is shown in Table 3. There were no significant differences between the two groups, except for the rate of bleeding and the rate of revascularization at six months. Subacute thrombosis occurred in 1 of 176 patients (0.6 percent) in the angioplasty group and in 7 of 178 patients (3.9 percent) in the stent group (on day 2 in 1 patient, on day 3 in 2, and on days 4, 8, 13, and 18 in 1 each). Thrombolytic therapy was given to one patient, angioplasty was per-

TABLE 2. CORONARY ANGIOGRAPHIC CHARACTERISTICS BEFORE AND AFTER INTERVENTION.*

| CHARACTERISTIC | ANGIOPLASTY GROUP (N=176) | STENT GROUP (N=178) | P VALUE |
|------------------------------------------|---------------------------|---------------------|---------|
| Reference diameter (mm) | | | |
| Before intervention | 3.04±0.26 | 3.01±0.32 | 0.34 |
| After angioplasty | 3.10±0.30 | 3.06±0.27 | 0.19 |
| After stenting | — | 3.13±0.26 | — |
| At 6 mo | 3.02±0.30 | 3.07±0.31 | 0.13 |
| Minimal luminal diameter (mm) | | | |
| Before intervention | 1.03±0.40 | 1.04±0.42 | 0.82 |
| After angioplasty | 2.23±0.57 | 2.15±0.45 | 0.15 |
| After stenting | — | 3.02±0.43 | — |
| At 6 mo | 1.85±0.56 | 2.04±0.66 | 0.01 |
| Stenosis (% of luminal diameter) | | | |
| Before intervention | 66±13 | 64±14 | 0.17 |
| After angioplasty | 30±17 | 31±15 | 0.56 |
| After stenting | — | 6±14 | — |
| At 6 mo | 47±24 | 30±19 | <0.001 |
| Restenosis (% of patients) | 32 | 18 | 0.03 |
| Change in minimal luminal diameter (mm)† | | | |
| Immediate gain | 1.20±0.52 | 1.98±0.49 | <0.001 |
| Late loss | 0.38±0.57 | 0.98±0.68 | <0.001 |
| Late-loss index | 0.13±0.09 | 0.33±0.13 | <0.001 |
| Net gain | 0.82±0.55 | 1.00±0.43 | 0.01 |

*Plus-minus values are means ±SD.

†Immediate gain denotes the minimal luminal diameter immediately after the procedure minus the reference diameter before the procedure, late loss the minimal luminal diameter immediately after the procedure minus the diameter at follow-up, and net gain the minimal luminal diameter at follow-up minus the reference diameter before the procedure. The late-loss index is the late loss divided by the reference diameter before the procedure.

formed in three patients, combined therapy was performed in one patient, and both angioplasty and bypass surgery were performed in two patients. The duration of hospitalization was 3.2±2.5 days in the angioplasty group and 5.8±2.8 days in the stent group (P<0.001).

Late Clinical Follow-up

The rate of event-free survival (absence of death, myocardial infarction, and target-vessel revascularization) at 250 days was 72 percent in the angioplasty group and 84 percent in the stent group (P=0.04 by the log-rank test) (Fig. 2). Revascularization of the target lesion was performed in 42 of 158 patients (27 percent) in the angioplasty group and in 16 of 156 patients (10 percent) in the stent group (P=0.001).

DISCUSSION

In this study, the rate of restenosis in patients who had undergone one or more previous angioplasties was significantly reduced by coronary stenting, as compared with standard balloon angioplasty. As a consequence, the proportion of patients who required revascularization of the target vessel was smaller in the stent group (27 percent) than in the angioplasty group (10 percent).

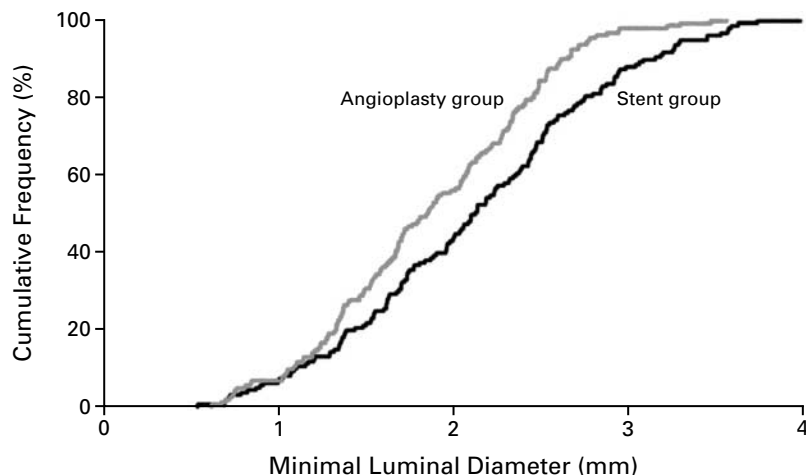


Figure 1. Minimal Luminal Diameter as Measured by Quantitative Coronary Angiography Six Months after Angioplasty Alone or Angioplasty with Stenting for the Treatment of Restenotic Lesions. The mean difference between the two groups was 0.19 mm.

TABLE 3. CUMULATIVE INCIDENCE OF CLINICAL EVENTS DURING HOSPITALIZATION AND AT SIX MONTHS.

| EVENT | ANGIOPLASTY GROUP (N=176) | STENT GROUP (N=178) | P VALUE | RELATIVE RISK (95% CI)* |
|----------------------------------|---------------------------------|---------------------------|------------|----------------------------|
| | no. of patients (%) | | | |
| Death | | | | |
| In hospital | 1 (0.6) | 2 (1.1) | 0.99 | 2.0 (0.2–22.1) |
| At 6 mo | 2 (1.1) | 2 (1.1) | 0.62 | 1.0 (0.1–7.1) |
| Q-wave myocardial infarction | | | | |
| In hospital | 1 (0.6) | 5 (2.8) | 0.22 | 5.1 (0.6–43.7) |
| At 6 mo | 1 (0.6) | 5 (2.8) | 0.22 | 5.1 (0.6–43.7) |
| Non-Q-wave myocardial infarction | | | | |
| In hospital | 1 (0.6) | 2 (1.1) | 0.99 | 2.0 (0.2–22.1) |
| At 6 mo | 1 (0.6) | 3 (1.7) | 0.62 | 3.0 (0.3–29.1) |
| Emergency bypass surgery | | | | |
| In hospital | 1 (0.6) | 2 (1.1) | 0.99 | 2.0 (0.2–22.1) |
| At 6 mo | 1 (0.6) | 2 (1.1) | 0.99 | 2.0 (0.2–22.1) |
| Elective bypass surgery | | | | |
| In hospital | 0 | 2 (1.1) | 0.48 | |
| At 6 mo | 1 (0.6) | 4 (2.2) | 0.37 | 4.0 (0.5–36.4) |
| Target-vessel revascularization | | | | |
| In hospital | 1 (0.6) | 5 (2.8) | 0.22 | 5.1 (0.6–43.7) |
| At 6 mo† | 42 (26.6) | 16 (10.3) | <0.001 | 0.3 (0.2–0.6) |
| Bleeding | | | | |
| Drop in hemoglobin, >3 g/dl | 1 (0.6) | 20 (11.2) | <0.001 | 0.1 (0.0–0.3) |
| Transfusion required | 1 (0.6) | 11 (6.2) | 0.01 | 0.1 (0.0–0.7) |
| Surgical repair required | 1 (0.6) | 10 (5.6) | 0.02 | 0.1 (0.0–0.8) |
| Retroperitoneal bleeding | 0 | 2 (1.1) | <0.001 | — |
| Gastrointestinal bleeding | 0 | 3 (1.7) | <0.001 | — |
| Any bleeding | 2 (1.1) | 20 (11.2) | <0.001 | 0.1 (0.0–0.4) |

*CI denotes confidence interval.

†Data were available for 158 patients in the angioplasty group and 156 in the stent group.

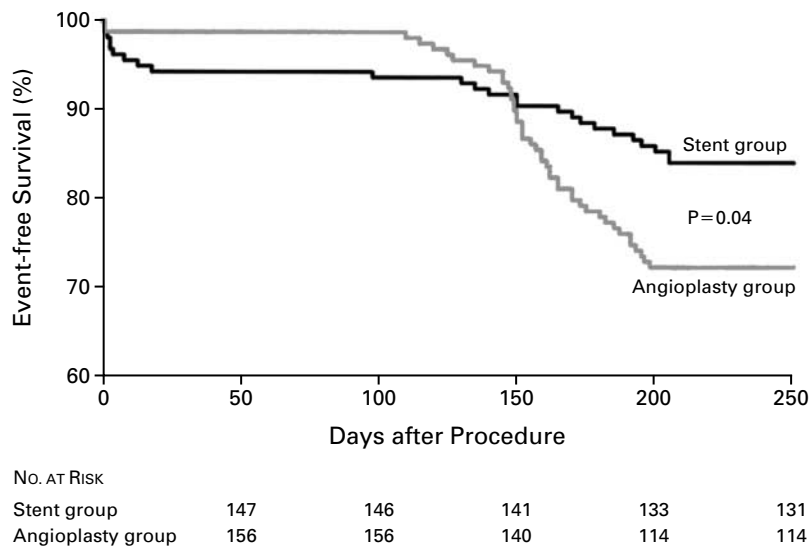


Figure 2. Event-free Survival (Absence of Death, Myocardial Infarction, Bypass Surgery, and Revascularization of the Target Vessel) within 250 Days after Angioplasty Alone or Angioplasty with Stenting.

These results agree with those of studies evaluating the effect of stenting in patients with new coronary stenoses who had not undergone prior angioplasty.^{19,20} Data from randomized studies comparing other treatment strategies for restenotic lesions are not available. In a study at one center, coronary stenting for restenosis was successful in 98 percent of patients,²⁷ which is similar to our success rate of 98.9 percent. The restenosis rate was 25 percent in the single-center study, which is higher than the rate in our study, even though the other study used higher balloon pressures (18 to 20 atmospheres) and intravascular ultrasonography in almost one third of the patients — two factors considered to be important advantages of the current stenting technique.^{27,28} The higher rate of restenosis in the single-center study may be related to the facts that the patients had longer lesions but smaller vessels and that multiple, overlapping stents were used.²⁷⁻³⁰ In a study of 113 patients who received Wallstents or Wiktor stents, the restenosis rate was 14 percent, and it was even lower (6 percent) when the observation period was limited to six months.³¹ These results are in accord with the rate of target-vessel revascularization (10 percent) in our study.³¹

As compared with the results of the Benestent and Stent Restenosis studies, which evaluated the use of angioplasty or stenting in patients with new lesions, in our study there was a similar immediate gain in the luminal diameter in the angioplasty group but a larger immediate gain in the stent group (Table 4).^{19,20} The late loss in luminal diameter in our angioplasty group was 0.38 ± 0.57 mm, which is similar to the results of the Benestent and Stent Restenosis studies (0.32 ± 0.47 and 0.38 ± 0.66 mm, respectively). The

net gain in the stent groups was also similar. These results make it clear that the larger the early gain in the luminal diameter, the greater the late loss due to neointimal proliferation.^{11,32-34}

Subacute thrombosis has been a major concern with stenting, with a frequency of approximately 3 percent in native vessels with new lesions and 2 to 4 percent in vessels with restenotic lesions.^{19,20,27,31} Despite our experience in controlling coagulation,³⁵ the rate of subacute stent thrombosis in our study was 3.9 percent, which is similar to the rates in other studies.^{19,20} The use of ticlopidine in combination with aspirin and the avoidance of oral anticoagulant therapy with warfarin resulted in a significantly lower incidence of subacute stent thrombosis, ranging from 1 to 2 percent.³⁶ With the use of heparin-coated stents, the rate of subacute thrombosis was less than 1 percent.³⁰

Acute occlusion of coronary vessels after balloon angioplasty is reported in 2 to 4 percent of patients.^{19,20,37,38} The fact that subacute thrombosis did not occur in any of the patients in our angioplasty group but did occur in 3.9 percent of the patients in the stent group may be related to the management protocol in the angioplasty group, since symptomatic dissection was an indication for stenting. The crossover rate in the angioplasty group was 6.8 percent, which is similar to the rates in previous studies (5.4 percent¹⁹ and 6.9 percent²⁰). Despite the crossover, our results were significant when the data were analyzed on an intention-to-treat basis.

A major concern has been bleeding complications due to intensive anticoagulation.^{19,20} Such complications have been effectively decreased by using high-pressure stenting and administering ticlopidine, an

TABLE 4. CORONARY ANGIOGRAPHIC RESULTS OF THE CURRENT STUDY AND OF TWO PREVIOUS STUDIES INVOLVING PATIENTS WITH NEW LESIONS.*

| | ANGIOPLASTY GROUP | | | STENT GROUP | | |
|-----------------------------------------|-------------------|-----------|-----------|-------------|-----------|-----------|
| | REST | BENESTENT | STRESS | REST | BENESTENT | STRESS |
| Reference diameter (mm) | | | | | | |
| Before intervention | 3.04±0.26 | 3.01±0.46 | 2.99±0.50 | 3.01±0.32 | 2.99±0.45 | 3.03±0.42 |
| After intervention | 3.10±0.30 | 3.09±0.44 | 2.99±0.46 | 3.13±0.26 | 3.16±0.43 | 3.05±0.40 |
| At follow-up | 3.02±0.30 | 3.05±0.49 | 2.98±0.49 | 3.07±0.31 | 2.96±0.48 | 3.00±0.41 |
| Minimal luminal diameter (mm) | | | | | | |
| Before intervention | 1.03±0.40 | 1.08±0.31 | 0.75±0.25 | 1.04±0.42 | 1.07±0.33 | 0.77±0.27 |
| After intervention | 2.23±0.57 | 2.05±0.33 | 1.99±0.47 | 3.02±0.43 | 2.48±0.39 | 2.49±0.43 |
| At follow-up | 1.85±0.56 | 1.73±0.55 | 1.56±0.65 | 2.04±0.66 | 1.82±0.64 | 1.74±0.60 |
| Stenosis (% of luminal diameter) | | | | | | |
| Before intervention | 66±13 | 64±10 | 75±8 | 64±14 | 64±10 | 75±9 |
| After intervention | 30±17 | 33±8 | 35±14 | 6±14 | 22±8 | 19±11 |
| At follow-up | 47±24 | 43±16 | 49±19 | 30±19 | 38±18 | 42±18 |
| Restenosis (% of patients) | 32 | 32 | 42 | 18 | 22 | 32 |
| Change in minimal luminal diameter (mm) | | | | | | |
| Immediate gain | 1.20±0.52 | 0.97±0.39 | 1.23±0.48 | 1.98±0.49 | 1.40±0.44 | 1.72±0.46 |
| Late loss | 0.38±0.57 | 0.32±0.47 | 0.38±0.66 | 0.98±0.68 | 0.65±0.57 | 0.74±0.58 |
| Net gain | 0.82±0.55 | 0.65±0.59 | 0.85±0.63 | 1.00±0.43 | 0.75±0.66 | 0.98±0.62 |

*REST denotes the Restenosis Stent trial, and STRESS the Stent Restenosis Study. Data for the Benestent study are from Serruys et al.,¹⁹ and data for STRESS are from Fischman et al.²⁰ Plus-minus values are means ±SD.

approach that makes anticoagulant therapy unnecessary.^{30,35} In our study, bleeding was the main drawback of coronary stenting for restenotic lesions.

Because of anticoagulant therapy, patients who underwent stenting stayed in the hospital longer than those who underwent angioplasty. This result is in agreement with the results of previous studies (mean hospital stays of 2.8 and 3.1 days after percutaneous transluminal coronary angioplasty and of 5.8 and 8.5 days after stenting).^{19,20} In our study, the rate of event-free survival was significantly lower in the angioplasty group than in the stent group. In the studies involving patients with new lesions, the rates of event-free survival were also lower in the angioplasty groups than in the stent groups: 76 percent as compared with 81 percent²⁰ and 70 percent as compared with 80 percent.¹⁹ Although there was excessive bleeding in our stent group, results with regard to the clinical end points of death, myocardial infarction, bypass surgery, and repeated revascularization favored stenting. There was an early risk of acute or subacute thrombosis but a late benefit when stenting was used in vessels with restenotic lesions.

In conclusion, as compared with standard balloon angioplasty, elective coronary stent placement had a higher clinical success rate with a lower incidence of restenosis and target-vessel revascularization. The reduction in the incidence of restenosis was associated with a lower rate of cardiac events despite a higher incidence of hemorrhagic complications and acute and subacute stent thrombosis. Coronary stenting can

be recommended for patients with restenosis after angioplasty.

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APPENDIX

The following institutions and investigators, in addition to the authors, participated in the Restenosis Stent trial: *Coronary Angiographic Laboratory*, University of Essen, Essen, Germany — M. Haude; *Data Coordinating Center*, Department of Cardiology, University of Essen, Essen, Germany — M. Haude, R. Krüger, and V. Schwarz; *Monitoring* — A. Piwinski, Hamburg, Germany; *Steering Committee* — R. Erbel, M. Haude, H.W. Höpp, and B. Heublein; *Study Investigators* — C. Macaya, Hospital Clinico San Carlos, Madrid; M. Nobuyoshi, Kokura Memorial Hospital, Kitakyushu, Japan; P. Hanrath and J. vom Dahl, University of Aachen, Aachen, Germany; H. Emanuelsson and O. Wiklund, Sahlgrenska University Hospital, Göteborg, Sweden; C. Hamm, University of Eppendorf, Hamburg, Germany; I.M. Penn, Vancouver Hospital, Vancouver, B.C., Canada; J. Ormiston, Green Lane Hospital, Auckland, New Zealand; J. Rustige, University of Ludwigshafen, Ludwigshafen, Germany; R. Simon, University Clinic Kiel, Kiel, Germany; and G. Kunkel, Friedrich Alexander University, Erlangen, Germany.

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