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## CORONARY ANGIOPLASTY WITH OR WITHOUT STENT IMPLANTATION FOR ACUTE MYOCARDIAL INFARCTION

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### ABSTRACT

**Background** Coronary-stent implantation is frequently performed for treatment of acute myocardial infarction. However, few studies have compared stent implantation with primary angioplasty alone.

**Methods** We designed a multicenter study to compare primary angioplasty with angioplasty accompanied by implantation of a heparin-coated Palmaz-Schatz stent. Patients with acute myocardial infarction underwent emergency catheterization and angioplasty. Those with vessels suitable for stenting were randomly assigned to undergo angioplasty with stenting (452 patients) or angioplasty alone (448 patients).

**Results** The mean ( $\pm$ SD) minimal luminal diameter was larger after stenting than after angioplasty alone ( $2.56\pm 0.44$  mm vs.  $2.12\pm 0.45$  mm,  $P<0.001$ ), although fewer patients assigned to stenting had grade 3 blood flow (according to the classification of the Thrombolysis in Myocardial Infarction trial) (89.4 percent, vs. 92.7 percent in the angioplasty group;  $P=0.10$ ). After six months, fewer patients in the stent group than in the angioplasty group had angina (11.3 percent vs. 16.9 percent,  $P=0.02$ ) or needed target-vessel revascularization because of ischemia (7.7 percent vs. 17.0 percent,  $P<0.001$ ). In addition, the combined primary end point of death, reinfarction, disabling stroke, or target-vessel revascularization because of ischemia occurred in fewer patients in the stent group than in the angioplasty group (12.6 percent vs. 20.1 percent,  $P<0.01$ ). The decrease in the combined end point was due entirely to the decreased need for target-vessel revascularization. The six-month mortality rates were 4.2 percent in the stent group and 2.7 percent in the angioplasty group ( $P=0.27$ ). Angiographic follow-up at 6.5 months demonstrated a lower incidence of restenosis in the stent group than in the angioplasty group (20.3 percent vs. 33.5 percent,  $P<0.001$ ).

**Conclusions** In patients with acute myocardial infarction, routine implantation of a stent has clinical benefits beyond those of primary coronary angioplasty alone. (N Engl J Med 1999;341:1949-56.)

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**P**ERCUTANEOUS transluminal coronary angioplasty for primary treatment after acute myocardial infarction has been demonstrated to be superior to thrombolytic therapy with regard to the restoration of normal coronary blood flow<sup>1</sup> and is associated with lower rates of recurrent ischemia, reinfarction, stroke, and death.<sup>2-4</sup> Primary angioplasty has clinical limitations, however. Abrupt closure occurs more often after primary angioplasty for emergency reperfusion than after elective procedures, and in 10 to 15 percent of patients ischemia recurs before hospital discharge.<sup>2,5</sup> Routine angiographic follow-up at six months has demonstrated reocclusion of the infarct-related artery in 10 to 15 percent of patients and restenosis in 35 to 40 percent.<sup>6,7</sup>

In our previous study of primary angioplasty, we found that the presence of coronary dissection or more than 30 percent residual stenosis was predictive of subsequent ischemic events.<sup>8</sup> Implantation of a coronary stent, which results in a large coronary lumen with few dissections, may reduce shear forces and platelet-thrombus deposition. Clinical benefits of this approach, as compared with primary angioplasty, may include lower rates of early ischemia as well as improved long-term patency and lower rates of restenosis of the infarct-related artery. However, the presence of a thrombus is common after acute myocardial in-

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fraction and may predispose patients to subacute thrombosis (thrombosis within the first month) after stenting.<sup>9</sup> In studies in animals, implantation of a heparin-coated Palmaz–Schatz stent was associated with 95 percent less platelet deposition than was implantation of an uncoated stent,<sup>10</sup> and in clinical trials, use of the coated stent was associated with low rates of subacute thrombosis.<sup>11–13</sup>

We therefore designed a multicenter, randomized trial to test the hypothesis that routine implantation of a stent, as compared with primary angioplasty alone, would result in larger luminal diameters after the procedure and would be associated with less angiographic evidence of restenosis and improved clinical outcomes at six months in patients with acute myocardial infarction.

## METHODS

### Selection of Patients

Patients were considered for the trial if they were at least 18 years old, if symptoms of myocardial infarction had begun less than 12 hours before written informed consent was requested, and if they had either ST-segment elevation of at least 1 mm in two or more contiguous electrocardiographic leads or a nondiagnostic electrocardiogram (including left bundle-branch block, a paced rhythm, ST-segment depression, or T-wave inversion) with documentation of acute myocardial infarction in the catheterization laboratory (with findings of high-grade coronary stenosis and associated left ventricular wall-motion abnormalities). Clinical criteria for exclusion were the previous administration of thrombolytic agents for the index infarction, current use of warfarin, stroke during the preceding month, renal failure, cardiogenic shock, remaining life expectancy of less than one year, childbearing potential (unless the result of a recent pregnancy test was negative), and known contraindications to aspirin, heparin, or ticlopidine. The study was conducted according to the principles of the Declaration of Helsinki, and all patients gave written informed consent.

### Catheterization and Study Procedure

The study protocol recommended that aspirin (250 mg administered intravenously or 325 mg administered as non-enteric-coated, chewable tablets), ticlopidine (500 mg orally), heparin (5000 to 10,000 IU intravenously), and (in the absence of contraindications) beta-blockers be given in the emergency department. Patients were then taken immediately to the cardiac catheterization laboratory, where coronary arteriography and left ventriculography were performed with the use of low-osmolar ionic contrast medium (ioxaglate, Mallinckrodt, St. Louis) to reduce the risk of thrombosis.<sup>14</sup> Once blood flow had been established (either spontaneously or by initial inflation of the balloon), the operator determined whether the patient qualified for randomization; the infarct-related vessel had to be a native coronary artery with a reference diameter of 3.0 to 4.5 mm and with one or more lesions that could be covered with one or two stents 15 mm in length. Patients were excluded from randomization if the operator decided that the patient would be better treated medically or surgically or if the infarct-related vessel had a high likelihood of requiring a stent. Patients were also excluded if the stent would protrude into the left main coronary artery (because of ostial lesions in the left anterior descending or circumflex artery), if large side branches ( $\geq 3.0$  mm in diameter) would be covered by the stent, or if tortuosity or calcification made it unlikely that the stent could be placed and expanded.

Once patients' eligibility for stenting had been established, randomization by telephone was performed in blocks of four according to clinical site. The diameters of the stent and of the balloon were

selected by visual estimation to achieve a balloon-to-artery ratio of 1:1. The protocol stent was a 15-mm, heparin-coated Palmaz–Schatz stent mounted on a balloon that incorporated a sleeved stent-delivery system (Cordis, Johnson & Johnson, Warren, N.J.). After deployment of the stent at 8 atm, a separate inflation at high pressure ( $\geq 16$  atm) was recommended. Heparin was administered throughout the procedure to maintain an activated clotting time of 350 seconds or longer. Administration of thrombolytic agents or platelet glycoprotein IIb/IIIa receptor inhibitors and the use of stents other than the protocol stent were discouraged, unless the vessel had a large thrombus, residual stenosis, or dissection that necessitated these interventions. In accordance with our standard protocol,<sup>15</sup> heparin infusion was recommended after primary angioplasty alone, but not after the placement of a heparin-coated stent unless the angiographic result was suboptimal ( $>10$  percent stenosis, residual thrombus, dissection, or absence of reflow) or unless there were other clinical indications (such as atrial fibrillation, left ventricular dysfunction, or multivessel disease).

Clinical events were monitored throughout the patient's hospital stay, and patients were evaluated at one month and at six months. Before performance of follow-up angiography at 6.5 months, investigators documented the Canadian Cardiovascular Society class of angina, the results of stress testing (if performed), and any electrocardiographic evidence of ischemia and reported to the coordinating center whether cardiac catheterization would have been performed if it had not been required by the protocol.

### Angiographic Analysis

Cineangiograms were obtained immediately after the procedure and at 6.5 months according to standard acquisition guidelines. The angiograms were submitted to the independent core angiography laboratories (Washington Hospital Center, Washington, D.C., and Cardialysis, Rotterdam, the Netherlands), and quantitative angiographic analysis was performed (CAAS II, Pie Medical, Maastricht, the Netherlands).<sup>16</sup> Standard morphologic criteria were used to characterize the complexity of the base-line lesions<sup>17</sup> and to identify complications that occurred during angiography.<sup>18</sup> Myocardial perfusion was graded according to the classification system of the Thrombolysis in Myocardial Infarction (TIMI) trial, in which blood flow with a grade of 3 indicates normal flow within the vessel.<sup>19</sup> The user-defined reference diameter and the minimal luminal diameter were used to calculate the percentage of stenosis. A value of 0 mm was assigned for the minimal luminal diameter in cases of total occlusion at base line or follow-up.

### End Points

Detailed case-report forms were completed by the clinical coordinators at each site. Independent data monitors traveled to each site to verify hospital records for all the patients. The primary end point of the study was the composite incidence of death, nonfatal reinfarction, disabling stroke, or target-vessel revascularization for treatment of ischemia (either percutaneous reintervention or bypass surgery) during the six-month follow-up period. Each component event in the primary end point was adjudicated by an independent clinical-events committee.

Reinfarction was defined as the recurrence of clinical symptoms (or the development of new electrocardiographic changes) accompanied by new elevation of the creatine kinase and creatine kinase MB enzyme levels. The level of creatine kinase required for a diagnosis of reinfarction depended on the interval from the index infarction: if new symptoms appeared within 48 hours of the index acute myocardial infarction, the necessary creatine kinase level was at least 1.5 times the previous value; after 48 hours, at least 3 times the upper limit of normal; and after subsequent bypass surgery, at least 5 times the upper limit of normal. A disabling stroke was defined as a stroke that resulted in severe limitation in the ability to perform daily activities or the inability to live independently. Ischemia during hospitalization was defined as a recurrence of symptoms accompanied by electrocardiographic changes, new elevation of creatine kinase levels, new hypotension, a new murmur, or sub-

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.\*

VARIABLE	STENT GROUP (N=452)	ANGIOPLASTY GROUP (N=448)	P VALUE
Age — yr	60.9±12.3	59.2±12.6	0.05
Male sex — % of patients	74.8	74.8	1.00
Diabetes — % of patients	15.9	14.1	0.69
Previous infarction — % of patients	10.8	11.8	0.45
Previous stroke — % of patients	4.6	2.9	0.33
Time in minutes — median (interquartile range)†			
From symptom onset to presentation	120 (74–233)	110 (60–210)	0.03
From presentation to catheterization	68 (42–112)	71 (45–110)	0.46
From presentation to first inflation	110 (77–162)	114 (80–153)	0.58
Infarct-related vessel — % of patients			0.55
Left anterior descending	39.8	43.5	
Right coronary	46.0	42.6	
Circumflex	13.7	13.6	
Graft‡	0.4	0.2	
Multivessel disease — % of patients	46.0	44.0	0.55
Ejection fraction — %	48.4±11.9	47.8±11.3	0.52

\*Plus-minus values are means ±SD.

†The interquartile range is the 25th to the 75th percentile.

‡The inclusion of patients requiring revascularization of a non-native vessel was a protocol deviation.

acute occlusion. Ischemia after discharge was defined as the development of Canadian Cardiovascular Society class II, III, or IV angina, abnormal results on an exercise test, or both. The need for target-vessel revascularization was attributed to ischemia if one or more of these components of ischemia were determined to be present by the clinical-events committee.

Secondary end points included the percentage of stenosis, the minimal luminal diameter, and the TIMI blood-flow grade immediately after the procedure; clinical events during the 30 days after the procedure; and minimal luminal diameter, restenosis ( $\geq 50$  percent stenosis), and reocclusion (TIMI grade 0 or 1 flow in a vessel that was previously patent) at 6 months. Major bleeding was defined as the need for surgical vascular repair, the need for transfusion of 2 or more units of blood, retroperitoneal or intracranial bleeding, or fatal bleeding. Hematoma, changes in the hematocrit, or both were considered to constitute minor bleeding.

### Statistical Analysis

Enrollment of 900 patients randomly assigned to either primary angioplasty alone or primary angioplasty accompanied by stent implantation, with a two-sided type I error rate of 0.05, yielded 90 percent power to detect a decrease in the incidence of the primary end point, from 30 percent after primary angioplasty to 20 percent after stenting. Comparisons between the two treatment groups were performed on an intention-to-treat basis, unless otherwise specified. For comparisons between the groups, the chi-square test (or, if there were fewer than five expected observations, Fisher's exact test) was used. For comparisons of continuous variables, analysis of variance was used according to the type of data and their distribution. Variables pertaining to the time elapsed before events were analyzed by the Kaplan-Meier method. Two-sided P values are reported.

## RESULTS

### Base-Line Characteristics and Immediate Results

Over an 11-month enrollment period, 1458 patients with acute myocardial infarction were screened at 62 sites in several countries. Of these 1458 patients,

900 were randomly assigned to one of two treatment groups: 452 to angioplasty and implantation of a heparin-coated Palmaz-Schatz stent and 448 to primary angioplasty alone. Of the remaining 558 patients, who were enrolled in a parallel registry, 170 did not undergo angioplasty and 388 underwent percutaneous revascularization (stent implantation in 162 and angioplasty in 226). The most common reasons for excluding these patients from enrollment were vessel size less than 3.0 mm or greater than 4.5 mm in diameter, vessel tortuosity, or a perceived need for stenting.

The base-line characteristics of the two groups were well matched, with the exception that patients in the stent group were slightly older (mean [ $\pm$ SD] age, 60.9±12.3 years, vs. 59.2±12.6 years in the angioplasty group;  $P=0.05$ ) (Table 1). The use of adjunctive medications is reported in Table 2. High doses of heparin resulted in a median activated clotting time of 388 seconds in both groups. The rate of use of intracoronary thrombolytic agents (in 0.4 percent of the stent group and 0.2 percent of the angioplasty group) and of abciximab (5.8 percent and 4.5 percent, respectively) was low in both groups.

Of the patients randomly assigned to stent implantation, 0.9 percent did not receive a heparin-coated stent, because of lack of availability of this type of stent, and in 1.5 percent the stent could not be deployed. Therefore, 98 percent of the patients in the stent group received their assigned therapy. Of the patients randomly assigned to angioplasty, 15 percent crossed over to treatment with a commercially available stent, because of suboptimal angiographic re-

**TABLE 2.** USE OF ADJUNCTIVE MEDICATIONS.

MEDICATION	STENT GROUP (N=452)	ANGIOPLASTY GROUP (N=448)	P VALUE
Aspirin (% of patients)	98.9	99.3	0.73
Ticlopidine (% of patients)	93.1	87.5	<0.01
Ioxaglate contrast (% of patients)	98.0	97.3	0.52
Median activated clotting time with heparin (sec)	388	388	1.0
Thrombolytic agent (% of patients)	0.4	0.2	1.0
Abciximab (% of patients)	5.8	4.5	0.45

sults. Only 0.2 percent of the patients in each group required emergency bypass surgery.

On the basis of core-laboratory analysis of the angiograms obtained immediately after the procedure, stenting resulted in a larger minimal luminal diameter, less residual stenosis, and fewer dissections than angioplasty alone, although stenting was associated with a trend toward a slightly lower incidence of TIMI grade 3 flow (Table 3). The rate of success according to angiographic criteria (<50 percent stenosis and TIMI grade 2 or 3 flow) in the stent group was similar to that in the angioplasty group (99.3 percent and 98.4 percent, respectively;  $P=0.22$ ). When the criteria were narrowed to include only TIMI grade 3 flow, angiographic success in the stent group remained similar to that in the angioplasty group (89.4 percent and 91.6 percent, respectively;  $P=0.30$ ).

### Events during Hospitalization and during the First Month

Heparin was used less frequently in patients assigned to stent implantation than in patients assigned to angioplasty alone (37 percent vs. 88 percent,  $P<0.001$ ); however, major bleeding (5.1 percent and 3.8 percent, respectively;  $P=0.42$ ) and minor bleeding (2.7 percent and 4.9 percent, respectively;  $P=0.08$ ) occurred with similar frequency in the two groups. The rates of recurrent ischemia during hospitalization were also similar in the stent and angioplasty groups (2.9 percent and 4.0 percent, respectively;  $P=0.37$ ), and overall, the median lengths of the hospital stay were identical (four days in each group), although in the United States, patients assigned to stenting were discharged an average of one day earlier than patients assigned to angioplasty.

Clinical events that occurred during the first month after intervention are listed in Table 4. Target-vessel revascularization to treat ischemia was needed less frequently in the stent group than in the angioplasty group (1.3 percent vs. 3.8 percent,  $P=0.02$ ), but there were no significant differences between the two groups in the rates of death, reinfarction, or disabling stroke. Subacute thrombosis occurred infrequently in both the stent and the angioplasty groups (0.9 percent and 1.1 percent, respectively;  $P=0.75$ ).

### Late Follow-up

The primary combined end point of death, reinfarction, disabling stroke, or target-vessel revascularization for ischemia occurred during the first six months after intervention in 12.6 percent of patients in the stent group and 20.1 percent of those in the an-

**TABLE 3.** RESULTS OF CORE-LABORATORY ANALYSIS OF ANGIOGRAMS IMMEDIATELY AFTER THE PROCEDURE AND AT 6.5 MONTHS.\*

VARIABLE	STENT GROUP	ANGIOPLASTY GROUP	P VALUE
After procedure (884 patients)†			
Immediate gain (mm)	2.21	1.78	<0.001
Minimal luminal diameter (mm)	2.56±0.44	2.12±0.45	<0.001
Residual stenosis (%)	11.1±11.6	25.1±11.9	<0.001
Dissection (% of patients)	11.9	30.8	<0.001
TIMI grade 3 flow (% of patients)	89.4	92.7	0.10
At 6.5 months (689 patients)†			
Minimal luminal diameter (mm)	1.81±0.70	1.58±0.76	<0.001
Residual stenosis (%)	35.6±22.2	44.7±23.5	<0.001
Restenosis (% of patients)	20.3	33.5	<0.001
Late loss (mm)	0.76	0.54	<0.001
Loss index (mm)	0.37	0.31	0.045
TIMI grade 3 flow (% of patients) (n=696)	90.1	86.3	0.13
Reocclusion (n=696)	5.1	9.3	0.04

\*Plus-minus values are means ±SD. Immediate gain is the minimal luminal diameter immediately after the procedure minus the minimal luminal diameter at base line. Late loss is the minimal luminal diameter immediately after the procedure minus the minimal luminal diameter at follow-up. The loss index is the late loss divided by the immediate gain.

†The number of patients is the number for whom angiograms were available and could be analyzed.

TABLE 4. CLINICAL EVENTS AT ONE AND SIX MONTHS.

EVENT	STENT GROUP (N=452)	ANGIOPLASTY GROUP (N=448)	P VALUE
	% of patients		
One month			
Death	3.5	1.8	0.15
Reinfarction	0.4	1.1	0.29
Disabling stroke	0.2	0.2	1.00
Target-vessel revascularization for ischemia	1.3	3.8	0.02
Combined end point	4.6	5.8	0.46
Six months			
Death	4.2	2.7	0.27
Reinfarction	2.4	2.2	1.00
Disabling stroke	0.2	0.2	1.00
Target-vessel revascularization for ischemia	7.7	17.0	<0.001
Combined end point	12.6	20.1	<0.01

angioplasty group ( $P<0.01$ ), a difference due entirely to the different rates of target-vessel revascularization in the two groups (Table 4). The divergence in the rates of clinical events occurred predominantly between one and six months after the index procedure (Fig. 1). Even though many patients in the angioplasty group underwent revascularization before the six-month clinical follow-up, the incidence of angina at six months in the stent group was still lower than that in the angioplasty group (11.3 percent vs. 16.9 percent,  $P=0.02$ ).

Follow-up angiograms obtained at 6.5 months demonstrated that patients assigned to stent implantation continued to have a larger minimal luminal diameter than those assigned to angioplasty alone ( $1.81\pm 0.70$  mm vs.  $1.57\pm 0.75$  mm,  $P<0.001$ ), as well as less residual stenosis ( $35.6\pm 22.2$  percent vs.  $44.7\pm 23.5$  percent,  $P<0.001$ ) (Table 3 and Fig. 2). As a result of these differences, the rate of restenosis in the stent group was lower than that in the angioplasty group (20.3 percent vs. 33.5 percent,  $P<0.001$ ). Moreover, reocclusion of the infarct-related artery occurred less frequently in patients assigned to stenting (5.1 percent, vs. 9.3 percent in the angioplasty group;  $P=0.04$ ).

## DISCUSSION

In this study of 900 patients with acute myocardial infarction, angioplasty combined with implantation of a heparin-coated Palmaz-Schatz stent resulted in better event-free survival than did primary angioplasty alone, as assessed by analysis of the combined end point of death, reinfarction, disabling stroke, or target-vessel revascularization for treatment of ischemia. The lower incidence of the combined end point in the stent group was attributable entirely to the lower rate of revascularization procedures in this group,

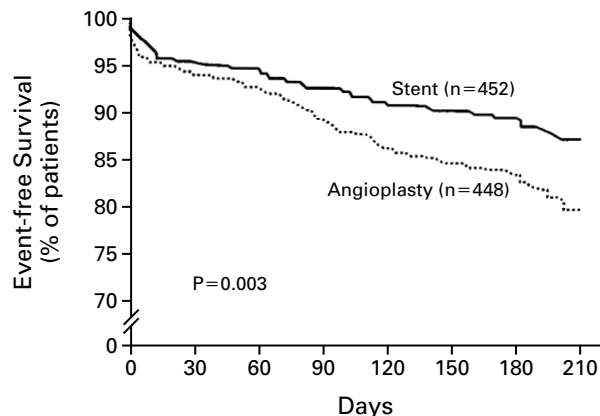
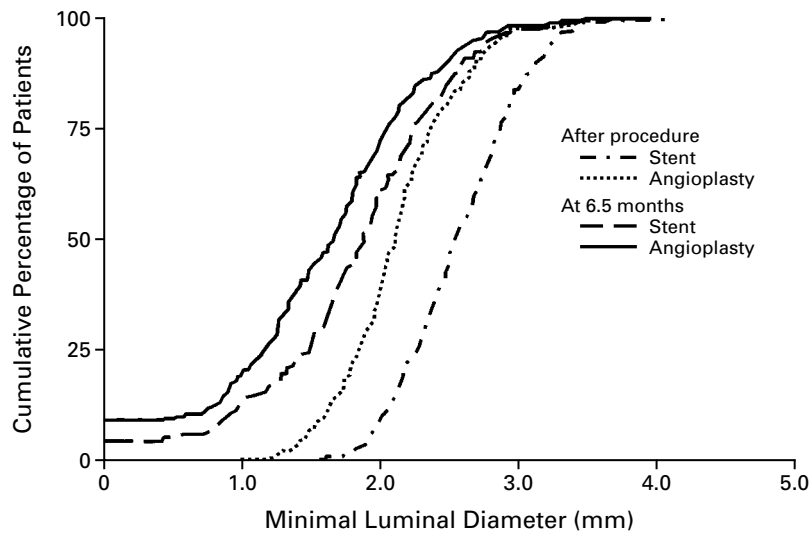


Figure 1. Event-free Survival According to Treatment Group.

Event-free survival was greater in the group of patients assigned to implantation of a heparin-coated stent than in the group assigned to primary angioplasty alone ( $P=0.003$  by the log-rank test). This difference was due to the lower proportion of patients in the stent group who underwent target-vessel revascularization for ischemia. Events (other than death) included reinfarction, disabling stroke, and target-vessel revascularization for ischemia.

an advantage presumably resulting from a larger coronary lumen and a lower frequency of dissections. The reduced need for revascularization is consistent with the results of smaller trials of stent implantation for acute myocardial infarction.<sup>20-22</sup> The improved outcomes that we observed after primary angioplasty for acute myocardial infarction, in comparison with previously reported outcomes, parallel those others have observed after elective angioplasty.<sup>23</sup> Unlike other studies, our trial did not reveal any difference at one month or six months in rates of reinfarction between patients assigned to stenting and those assigned to angioplasty. A nonsignificantly higher mortality rate was observed in the stent group, perhaps accounted for in part by the trend toward lower rates of TIMI grade 3 flow in the stent group.<sup>1</sup> However, the similarity in rates of reinfarction between the two groups may also have been due to the extremely low rate of events in the angioplasty group, with rates of death and reinfarction during hospitalization 50 percent lower than those observed in previous trials.<sup>2-7</sup> Moreover, the incidence of the combined end point six months after primary angioplasty was 33 percent lower than anticipated (approximately 20 percent instead of 30 percent). The crossover to stenting of 15 percent of the patients who had been randomly assigned to angioplasty may have contributed to the low rate of events in the angioplasty group.

Previous studies demonstrated that after angioplasty, the presence of residual stenosis of more than 30 percent or the presence of dissection was associated with recurrent ischemia and reocclusion of the infarct-related vessel.<sup>8</sup> In our study, stent implantation result-



**Figure 2.** Cumulative Distribution of Minimal Luminal Diameters Immediately after Revascularization and at 6.5 Months.

The minimal luminal diameter as measured by quantitative coronary angiography is shown for the 340 patients in the stent group and the 334 patients in the angioplasty group for whom matched views (at base line and follow-up) were available. At both times, the minimal luminal diameter was greater in the stent group than in the angioplasty group ( $2.57 \pm 0.42$  mm vs.  $2.13 \pm 0.44$  mm after the procedure and  $1.81 \pm 0.70$  mm vs.  $1.57 \pm 0.75$  mm at 6.5 months).

ed in a larger coronary lumen and fewer dissections. However, there was a disturbing trend toward lower rates of TIMI grade 3 blood flow after routine stenting than after primary angioplasty. This trend may be due to chance, since the rates of TIMI grade 3 flow were greater than 90 percent in other trials of stenting for acute myocardial infarction.<sup>13,20-22,24</sup> Moreover, it was reassuring to find that this trend had reversed itself in favor of the stent group at follow-up angiography at 6.5 months. However, it is possible that the longer time from the onset of symptoms of myocardial infarction to admission in the stent group contributed to the greater incidence of “no reflow” (less than TIMI grade 3 flow) in this group; it is also possible that the bulky design of the Palmaz-Schatz stent may have caused thrombus to embolize or that thrombus may have extruded through the struts and embolized during subsequent high-pressure balloon inflations. A trial to determine whether this finding of a reduced rate of TIMI grade 3 flow can be reproduced, and if so, whether the reduction can be prevented with abciximab, is under way.

Although it was anticipated that discontinuation of heparin early after the procedure would reduce the incidence of bleeding and allow earlier discharge from the hospital, these benefits were not observed in the stent group. The incidence of bleeding in our trial was low, and if we applied the definition of major bleeding used in trials of elective intervention,<sup>25,26</sup> the rate dropped to 3 percent; thus, a larger sample may

be required to show a benefit associated with the discontinuation of heparin after the procedure. Likewise, the length of hospitalization in both groups was shorter than that in previous trials, especially in the United States, where the length of hospitalization (in this study, a median of only three days) is often dictated by managed care or other insurance considerations. Physicians in the United States may have reached a psychological or perceived medicolegal barrier to earlier discharge.

The divergence between the stent group and the angioplasty group in the rate of clinical events occurred between one and six months after intervention, a finding consistent with the known time course of restenosis. As expected, we found a lower rate of restenosis in the stent group than in the angioplasty group. Interestingly, the rate of restenosis after emergency implantation of a stent for acute myocardial infarction was similar to that observed in elective cases. This suggests that thrombus and activated platelets already present at the time of acute myocardial infarction may not influence the risk of restenosis, or perhaps that a reduction in platelet deposition due to the use of the heparin-coated stent,<sup>10</sup> as compared with an uncoated stent, had a positive effect on the rate of restenosis.

Reocclusion at 6.5 months was found in only 5.1 percent of patients who were randomly assigned to receive the stent. This result compares favorably with the approximately 30 percent rate of late reocclusion

after thrombolysis<sup>27-29</sup> and the 13 percent rate after primary angioplasty<sup>3,6,7</sup> in previous trials. In the current trial, even the angioplasty group had rates of reocclusion lower than those previously reported, suggesting a beneficial role of contemporary pharmacologic regimens, close monitoring of activated clotting times, and availability of stenting as a treatment option in case of suboptimal results.<sup>15</sup>

This trial did not allow us to assess the importance of the heparin coating of the stent relative to that of its metal scaffolding. It is possible that the scaffolding effect of the stent, which enlarges the lumen and seals dissections, accounted for most of the benefit associated with stenting. However, the ability of a heparin coating to reduce platelet deposition and thrombus formation<sup>21</sup> may have also contributed to the low rate of subacute thrombosis in the group of patients who received a stent.

It may be asked whether the results of this trial make it unethical to withhold stenting from patients with myocardial infarction. The answer to that question depends on what end point is considered. Clearly, stenting reduces the incidence of ischemia and the need for subsequent target-vessel revascularization. Ischemia, reocclusion, and restenosis contribute to morbidity, rehospitalization, and costs and are important considerations. However, we have no evidence that the empirical implantation of a stent, as compared with angioplasty alone, will reduce the most important complications of myocardial infarction: reinfarction, death, and stroke. Given the trend toward lower rates of TIMI grade 3 blood flow, additional trials should be performed and long-term cost effectiveness determined before routine stenting can be recommended as the standard of care for patients with myocardial infarction.

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## APPENDIX

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