

CORONARY STENTING PLUS PLATELET GLYCOPROTEIN IIb/IIIa BLOCKADE  
COMPARED WITH TISSUE PLASMINOGEN ACTIVATOR  
IN ACUTE MYOCARDIAL INFARCTION

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IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION STUDY INVESTIGATORS\*

**ABSTRACT**

**Background** Prevention of myocardial damage is the main goal of all reperfusion therapies in patients with acute myocardial infarction. The relative efficacy of various reperfusion strategies is under intensive investigation. We assessed whether coronary stenting combined with the blockade of platelet glycoprotein IIb/IIIa receptors produces a greater degree of myocardial salvage than fibrinolysis with an accelerated infusion of alteplase, a tissue plasminogen activator.

**Methods** A total of 140 patients were enrolled in the randomized trial; 71 were assigned to receive a stent plus abciximab, and 69 to receive intravenous alteplase. The primary end point was the degree of myocardial salvage, determined by means of serial scintigraphic studies with technetium Tc 99m sestamibi. The secondary end point was a composite of death, reinfarction, and stroke within six months after randomization.

**Results** In the group that received a stent plus abciximab, the median size of the final infarct was 14.3 percent of the left ventricle (25th and 75th percentiles, 6.8 and 24.5 percent), as compared with a median of 19.4 percent (25th and 75th percentiles, 7.9 and 34.2 percent) in the alteplase group ( $P=0.02$ ). This difference was due to the larger salvage index (the percentage of the left ventricle that was salvaged, divided by the percentage that was compromised by the initial perfusion defect) in the stent group: 0.57 (25th and 75th percentiles, 0.35 and 0.69), as compared with 0.26 (25th and 75th percentiles, 0.09 and 0.61;  $P<0.001$ ). The cumulative incidence of death, reinfarction, or stroke at six months was lower in the stent group than in the alteplase group (8.5 vs. 23.2 percent,  $P=0.02$ ; relative risk, 0.34; 95 percent confidence interval, 0.13 to 0.88).

**Conclusions** In patients with acute myocardial infarction, coronary stenting plus abciximab leads to a greater degree of myocardial salvage and a better clinical outcome than does fibrinolysis with a tissue plasminogen activator. (N Engl J Med 2000;343:385-91.)

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PATIENTS with acute myocardial infarction benefit markedly from the restoration of coronary blood flow in the infarct-related vessel, and myocardial salvage is the principal mechanism of this benefit.<sup>1</sup> The unequivocal demonstration of the advantages of early fibrinolysis in patients with acute myocardial infarction<sup>2,3</sup> led to the widespread use of this reperfusion strategy. Subsequently, randomized trials indicated that primary percutaneous transluminal coronary angioplasty (PTCA) may be superior to fibrinolysis with regard to the early<sup>4-6</sup> and late<sup>7,8</sup> clinical outcomes. However, the only randomized study that specifically assessed myocardial salvage found a small but nonsignificant difference in favor of primary PTCA as compared with fibrinolysis.<sup>9</sup> On the other hand, registry studies have called into question the superiority of primary PTCA in general clinical practice.<sup>10,11</sup> Because of these inconclusive findings and the broader availability of fibrinolysis, this strategy is actually the most common therapy for patients with acute myocardial infarction who present with ST-segment elevation within the first 12 hours after the onset of symptoms.<sup>12</sup>

Coronary stenting is superior to conventional PTCA for the majority of patients with stable or unstable angina pectoris,<sup>13</sup> and coronary stenting is playing an increasing part in the treatment of patients with acute myocardial infarction.<sup>14-16</sup> Blockade of platelet glycoprotein IIb/IIIa receptors with abciximab has improved the outcome of patients with acute myocardial infarction<sup>17,18</sup> as well as those with stable or unstable angina<sup>19</sup> who are undergoing percutaneous coronary interventions. The combination of stenting and abciximab is effective in improving both epicardial blood flow<sup>20</sup> and microcirculation,<sup>18</sup> which, in turn, may increase the extent of myocardial salvage in patients with acute myocardial infarction.

We conducted a randomized trial to assess whether stenting combined with blockade of glycoprotein IIb/IIIa receptors leads to a greater degree of myo-

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cardial salvage and better clinical outcome in patients with acute myocardial infarction than fibrinolysis with an accelerated infusion of alteplase, a recombinant plasminogen activator.

## METHODS

### Patients

The study was conducted between December 1997 and August 1999. Patients eligible for this study were those who presented within 12 hours after the onset of symptoms, had chest pain for at least 20 minutes, and had ST-segment elevation of at least 0.1 mV in two or more limb leads or at least 2 mV in two or more contiguous precordial leads on the surface electrocardiogram. We excluded patients who had a recent history of stroke (within three months), those with active bleeding or bleeding diathesis, those with a recent history of trauma or major surgery (within a month), those with suspected aortic dissection, those with noncompressible vascular punctures, those receiving oral anticoagulant therapy with coumarin derivatives, and those with severe, uncontrolled hypertension (defined as a systolic blood pressure of more than 180 mm Hg that was unresponsive to therapy). The study protocol was approved by the institutional ethics committee.

### Study Protocol

After providing informed consent, patients who fulfilled the entry criteria were randomly assigned to one of the treatment strategies — intravenous fibrinolysis or coronary stenting plus abciximab — according to a computer-generated randomization scheme. All patients received 500 mg of aspirin and 5000 U of heparin intravenously in the emergency room. Immediately after randomization but before the initiation of the assigned therapy, patients received an intravenous injection of 27 mCi (1000 MBq) of technetium Tc 99m sestamibi. Single-photon-emission computed tomography was performed within six to eight hours after the injection of the radionuclide. A follow-up scintigraphic study was scheduled to be performed approximately 10 days after treatment.

Patients assigned to intravenous fibrinolysis received a bolus dose of 15 mg of alteplase (Actilyse, Boehringer Ingelheim, Ingelheim, Germany) followed by a 90-minute infusion in which 0.75 mg per kilogram of body weight (maximal dose, 50 mg) was given over a period of 30 minutes, followed by 0.5 mg per kilogram (maximal dose, 35 mg) over a period of 60 minutes. They also received intravenous heparin for a period of 48 hours; the initial dose was 1000 U per hour, and the dose was adjusted to achieve an activated partial-thromboplastin time between 60 and 85 seconds. A regimen consisting of 100 mg of aspirin twice a day was given indefinitely.

Placement of coronary stents in patients assigned to this treatment strategy was carried out according to our previously described method.<sup>21</sup> The stent implanted was the Multi-link stent (Guidant, Advanced Cardiovascular Systems, Santa Clara, Calif.). During the intervention the patients received an additional dose of 2500 U of heparin intraarterially as well as abciximab (ReoPro, Lilly Deutschland, Bad Homburg, Germany), given as a bolus of 0.25 mg per kilogram followed by a continuous infusion at a rate of 10  $\mu$ g per minute for 12 hours. Postinterventional antithrombotic therapy consisted of ticlopidine, given at a dose of 250 mg twice a day for four weeks, and aspirin, given at a dose of 100 mg twice a day indefinitely.

### Radionuclide Studies

Multihead camera systems with low-energy, high-resolution collimators were used for the radionuclide studies. Images were acquired in a 64-by-64 matrix with an acquisition time of 40 seconds per image. Dedicated software was used to generate transverse slices. A volumetric sampling tool was applied to create polar maps of the relative distribution of activity throughout the left ventricle.<sup>22</sup> Each polar map was adjusted for its own maximal value. The

size of the defect was calculated with the use of a threshold of 50 percent, which was derived from studies that used a phantom, according to previously described methods.<sup>23,24</sup> This method allowed us to calculate the following: the percentage of the left ventricle that was compromised by the initial perfusion defect; the size of the infarct (as a percentage of the left ventricle) at the time of follow-up scintigraphy; the degree of myocardial salvage (as a percentage of the left ventricle), calculated as the size of the initial perfusion defect minus the final size of the infarct; and the salvage index, calculated as the percentage of the left ventricle that was salvaged, divided by the percentage that was compromised by the initial perfusion defect.

All measurements were performed in the scintigraphic core laboratory by operators who were unaware of the patients' assigned therapy. The mean ( $\pm$ SD) intraobserver and interobserver variations in the measurement of the size of the defect in this laboratory were  $2\pm 3$  percent and  $2\pm 3$  percent of the left ventricle, respectively.

### Angiographic Evaluation

In patients assigned to the stent group, initial and postprocedural flow in the infarct-related artery was graded according to the Thrombolysis in Myocardial Infarction (TIMI) classification. Digital angiograms were analyzed off line in the angiographic core laboratory with an automated edge-detection system (CMS, Medis Medical Imaging Systems, Nuenen, the Netherlands).

### Study End Points and Definitions

The primary end point of the study was the salvage index. The secondary end point was a composite of death, reinfarction, and stroke within six months after randomization. The diagnosis of infarction was based on the findings of typical chest pain, new ST-segment changes, and an increase in the creatine kinase level of at least 50 percent over the trough level measured in at least two samples in which levels were at least 240 U per liter. The diagnosis of stroke required confirmation by computed tomography or magnetic resonance imaging of the head.

Other adverse events recorded were revascularization of the target vessel because of ischemia and major bleeding complications. Revascularization of the infarct-related artery through PTCA or coronary-artery bypass grafting was performed when symptoms or signs of ischemia were present when the patient was at rest or during exercise. A major bleeding complication was defined as any bleeding that caused hemodynamic compromise or required blood transfusion.

Levels of creatine kinase and its MB isoenzyme, hemoglobin levels, and the platelet count were determined before and 8, 16, and 24 hours after the treatment and daily thereafter until discharge. After discharge, the patients' clinical status was determined by means of a telephone interview at 30 days and a follow-up visit at 6 months or whenever a patient reported having symptoms.

### Statistical Analysis

The number of patients included in the study was based on the estimation of the sample size needed to identify a significant difference in the primary end point. In a pilot study of primary stenting in patients with acute myocardial infarction, we found that the average salvage index was  $0.55\pm 0.28$ . Assuming that the salvage index would be 0.40 in the fibrinolysis group, we estimated that 60 patients would be required in each group for the study to have a power of 80 percent to detect an absolute difference in the salvage index of 0.15 with a two-sided  $\alpha$  value of 0.05.<sup>25</sup> We allowed for the possibility that scintigraphic studies would be incomplete in some patients by including a total of 140 patients.

All analyses were performed according to the intention-to-treat principle. The data are presented as medians (with the 25th and 75th percentiles) or as counts or proportions. The differences between the groups were assessed with use of a two-sided chi-square test or Fisher's exact test for categorical data and the nonparametric Wilcoxon rank-sum test for continuous data. Survival was an

alyzed according to the Kaplan–Meier method. The relative risk of adverse events during the first six months after randomization was derived from proportional-hazards regression analysis. Differences in survival were also assessed for significance by means of the log-rank test. A two-tailed P value of less than 0.05 was considered to indicate statistical significance.

## RESULTS

Of the 140 patients enrolled, 71 were randomly assigned to undergo stenting and receive abciximab and 69 to receive intravenous alteplase. Only one patient in the stent group did not receive the assigned therapy; in this patient, the occluded left anterior descending artery opened during injection of the contrast medium, and no angiographically significant residual stenosis was visible. Table 1 shows the baseline characteristics of the two groups. Killip class 3 or 4 was found at presentation in 8.4 percent of the patients in the stent group and 2.9 percent of those in the alteplase group ( $P=0.29$ ). There was no significant difference between groups in the time from the onset of symptoms to admission, but there was a significant delay in providing the assigned therapy in the stent group. There were no significant differences between the groups in the proportions of patients who were receiving concomitant medications. Table 2 shows the initial and postprocedural angiographic characteristics of the patients who were assigned to undergo coronary stenting. Antegrade blood flow was fully restored (TIMI flow grade 3) in 95.8 percent of the patients who received a stent plus abciximab.

### Myocardial Salvage

The initial radionuclide study could not be performed in six patients in the stent group and seven in the alteplase group because of hemodynamic instability or for technical reasons. Of the six such patients in the stent group, three died soon after the procedure (one on day 1, one on day 3, and one on day 5), two underwent the follow-up radionuclide study (final infarct size, 29.7 percent and 3.0 percent of the left ventricle), and one did not undergo the follow-up study. Of the seven such patients in the alteplase group, three died soon after receiving the fibrinolytic therapy (two on day 1 and one on day 3), two underwent the follow-up radionuclide study (final infarct size, 20.9 percent and 15.7 percent of the left ventricle), and the other two did not undergo the follow-up study. Of the 127 patients who underwent the initial radionuclide study, 2 patients in each group did not undergo the follow-up study. Thus, 63 patients in the stent group (88.7 percent) and 60 patients in the alteplase group (87.0 percent,  $P=0.75$ ) underwent both the initial and the follow-up radionuclide studies that were required for the calculation of the primary end point. Only three of the patients in the stent group and four in the alteplase group underwent revascularization of the infarct-related artery between the initial and follow-up radionuclide studies.

TABLE 1. MAIN CHARACTERISTICS OF THE PATIENTS.\*

CHARACTERISTIC	STENT GROUP (N=71)	ALTEPLASE GROUP (N=69)
Age (yr)		
Median	57.8	60.9
25th and 75th percentiles	51.7, 70.2	51.6, 79.7
Female sex (%)	25.4	23.2
Arterial hypertension (%)	60.9	67.6
Diabetes (%)	21.1	18.8
Insulin therapy (%)	5.6	5.8
Current smoker (%)	52.1	40.6
Cholesterol level (mg/dl)†		
Median	198	182
25th and 75th percentiles	168, 224	160, 211
Prior myocardial infarction (%)	9.9	14.5
Prior CABG (%)	1.4	4.3
Anterior myocardial infarction (%)	47.9	47.8
Killip class (%)		
1	69.0	69.6
2	22.6	27.5
3	4.2	0
4	4.2	2.9
Systolic blood pressure (mm Hg)		
Median	140	140
25th and 75th percentiles	118, 150	121, 155
Diastolic blood pressure (mm Hg)		
Median	80	80
25th and 75th percentiles	70, 90	70, 90
Heart rate (beats/min)		
Median	71	72
25th and 75th percentiles	60, 80	60, 88
Time from onset of symptoms to admission (min)		
Median	150	150
25th and 75th percentiles	110, 277	85, 270
Time from admission to balloon inflation or initiation of alteplase therapy (min)‡		
Median	65	30
25th and 75th percentiles	53, 85	23, 40
Concomitant medications (%)		
Beta-blockers	85.9	87.0
ACE inhibitors	88.7	87.0
Nitrates	14.1	10.1
Calcium-channel blockers	4.2	4.3
Statins	83.1	84.1

\*CABG denotes coronary-artery bypass grafting, and ACE angiotensin-converting enzyme.

†To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

‡ $P<0.001$  for the comparison between groups.

Table 3 shows the results of scintigraphy. Although the size of the initial perfusion defect was similar in the two groups, the final size of the infarct was significantly smaller among patients in the stent group than among those in the alteplase group (14.3 percent vs. 19.4 percent of the left ventricle,  $P=0.02$ ). This difference was the result of a greater degree of myocardial salvage in the stent group (16.1 percent vs. 7.4 percent of the left ventricle,  $P<0.001$ ). There-

**TABLE 2.** ANGIOGRAPHIC CHARACTERISTICS OF THE 71 PATIENTS IN THE STENT GROUP AT BASE LINE AND AFTER STENTING.\*

CHARACTERISTIC	VALUE
Vessel involved (%)	
Left anterior descending coronary artery	47.9
Left circumflex coronary artery	11.3
Right coronary artery	39.4
Bypass graft	1.4
Initial TIMI flow grade (%)	
0	66.2
1	14.1
2	14.1
3	5.6
Final TIMI flow grade (%)	
0	1.4
1	2.8
2	0
3	95.8
Severity of coronary artery disease at base line (%)	
Single-vessel disease	47.9
Two-vessel disease	28.2
Three-vessel disease	23.9
Vessel size at base line (mm)	
Median	3.08
25th and 75th percentiles	2.8, 3.4
Initial minimal luminal diameter (mm)	
Median	0
25th and 75th percentiles	0, 0.26
Final minimal luminal diameter (mm)	
Median	2.92
25th and 75th percentiles	2.64, 3.34
Initial extent of stenosis (%)	
Median	100
25th and 75th percentiles	90, 100
Final extent of stenosis (%)	
Median	6.0
25th and 75th percentiles	0.7, 11.4
Maximal balloon pressure (atm)	
Median	13.5
25th and 75th percentiles	12, 15
Balloon-to-vessel ratio	
Median	1.05
25th and 75th percentiles	1.01, 1.09
Length of stented segment (mm)	
Median	21
25th and 75th percentiles	15, 32

\*TIMI denotes Thrombolysis in Myocardial Infarction.

fore, the primary end point of the trial — the salvage index — was significantly greater with stenting than with alteplase (0.57 vs. 0.26,  $P < 0.001$ ).

#### Clinical Outcome

Three patients in the stent group (4.2 percent) and five in the alteplase group (7.2 percent) died during the first 30 days after randomization. There were also two cases of nonfatal reinfarctions among patients in the stent group and four cases among patients in the alteplase group. Thus, the composite end point of death, reinfarction, or stroke at 30 days was reached in five patients in the stent group (7.0 percent) and nine patients in the alteplase group (13.0 percent). One patient in each group required urgent coronary-

artery bypass grafting during this period. Major bleeding complications were observed in three patients in the stent group and two in the alteplase group.

At six months, the incidence of death, reinfarction, or stroke (no cases of stroke were observed during follow-up) was 8.5 percent in the stent group, as compared with 23.2 percent in the alteplase group (relative risk, 0.34; 95 percent confidence interval, 0.13 to 0.88) (Fig. 1). The cumulative incidence of death during this period was 4.2 percent in the stent group and 13.0 percent in the alteplase group (relative risk, 0.31; 95 percent confidence interval, 0.08 to 1.16). Revascularization of the infarct-related artery was needed in 10.0 percent of the patients in the stent group and 34.9 percent of the patients in the alteplase group (relative risk, 0.24; 95 percent confidence interval, 0.11 to 0.57).

The primary and secondary end points were also analyzed in several subgroups. These results are given in Figure 2 and show the consistency of scintigraphic and clinical findings among the subgroups.

#### DISCUSSION

Our findings demonstrate that primary stenting combined with abciximab therapy results in a significantly greater degree of myocardial salvage than does fibrinolysis with an accelerated infusion of alteplase in patients with acute myocardial infarction. Although the base-line characteristics were similar in the two groups, patients who underwent stenting had a smaller final infarct size and a lower risk of major adverse clinical events during the six months after the primary treatment.

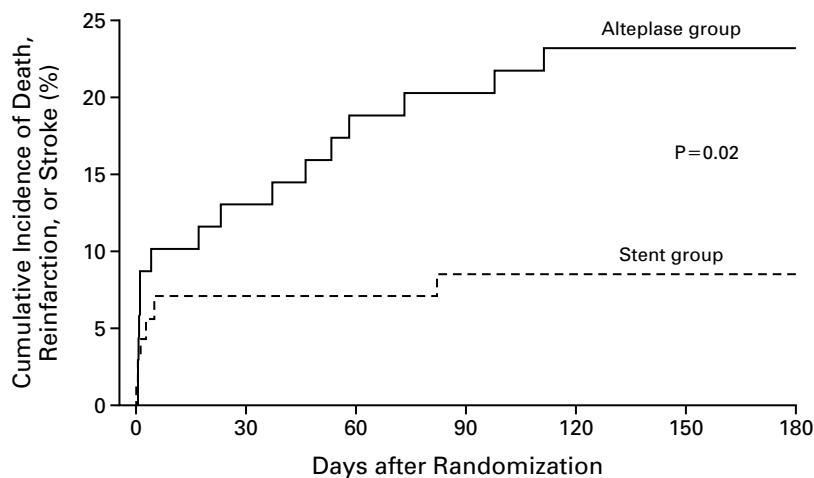
We used a sensitive, reliable, and practical technique to assess the degree of myocardial salvage. Because of its insignificant redistribution<sup>26</sup> after initial extraction,<sup>99mTc</sup>-sestamibi can be injected before the reperfusion treatment and imaging can be postponed until after the treatment, avoiding any delay in the treatment of patients with acute myocardial infarction. The accuracy of this method for the assessment of both the size of the initial defect and the size of the infarct after reperfusion has been validated in several studies.<sup>23,27</sup> The use of myocardial salvage as an end point in reperfusion trials is being advocated because of its potential prognostic value.<sup>28,29</sup>

The base-line characteristics of the patients in the alteplase group were representative of those treated with fibrinolysis in recent reperfusion trials, except for a slightly greater proportion of patients in Killip class 4 in our population. The 30-day mortality rate of 7.2 percent among the patients treated with alteplase is within the range of 6.2 to 7.5 percent reported in previous clinical trials of the same fibrinolytic agent.<sup>6,30-33</sup> The size of the initial perfusion defect is also similar to that quantified in the randomized trial conducted by Gibbons et al.<sup>9</sup> The use of alteplase in that study led, however, to a greater degree of myocardial sal-

TABLE 3. RESULTS OF SCINTIGRAPHY.\*

VARIABLE	STENT GROUP (N=63)		ALTEPLASE GROUP (N=60)		P VALUE
	MEDIAN	25TH AND 75TH PERCENTILES	MEDIAN	25TH AND 75TH PERCENTILES	
Size of initial perfusion defect (percentage of the LV)	31.5	18.6, 51.1	29.5	16.3, 45.2	0.45
Time from randomization to follow- up scintigraphic study (days)	10	8, 12	10	9, 12	0.75
Final infarct size (percentage of the LV)	14.3	6.8, 24.5	19.4	7.9, 34.2	0.02
Degree of myocardial salvage (percentage of the LV)	16.1	6.7, 26.1	7.4	1.9, 17.3	<0.001
Salvage index	0.57	0.35, 0.69	0.26	0.09, 0.61	<0.001

\*Initial and follow-up radionuclide studies were performed in 63 patients in the stent group and 60 patients in the alteplase group. The degree of myocardial salvage was calculated as the size of the initial perfusion defect minus the size of the final infarct. The salvage index was calculated by dividing the percentage of the left ventricle that was salvaged by the percentage that was compromised by the initial perfusion defect. LV denotes left ventricle.



No. AT RISK

Stent group	71	66	66	65	65	65	65
Alteplase group	69	60	56	55	53	53	53

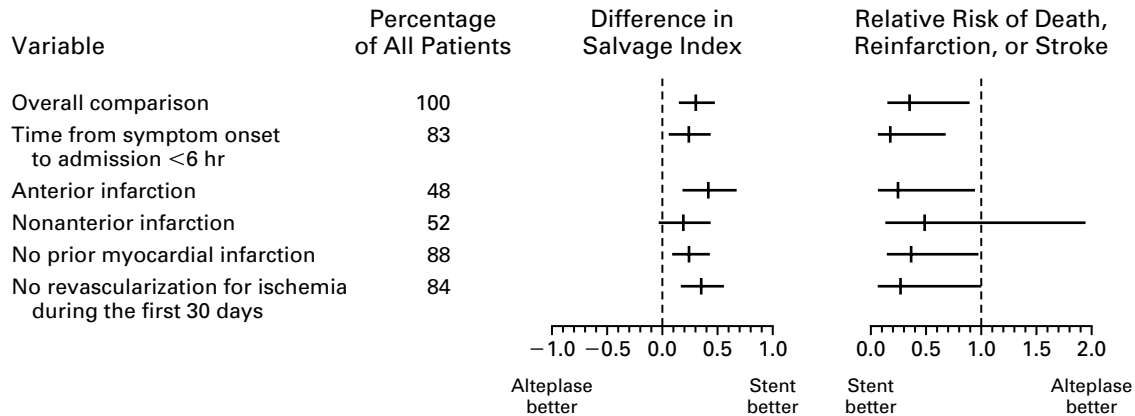
Figure 1. Kaplan-Meier Estimates of the Cumulative Incidence of Death, Reinfarction, or Stroke during the First Six Months after Randomization.

The log-rank test was used to calculate the P value.

vage than in our study. Two factors may account for this difference. First, the characteristics of the patients may have differed, since none of the patients enrolled in the fibrinolysis group in the study by Gibbons et al.<sup>9</sup> died during the six-month follow-up period. Second, 21 of the 56 patients (38 percent) who were assigned to fibrinolysis in the study by Gibbons et al.<sup>9</sup>

underwent angioplasty of the infarct-related vessel during hospitalization, a procedure that may have increased the degree of myocardial salvage, which was assessed before discharge.

In our study, patients assigned to stenting had base-line clinical characteristics that were similar to those of patients in the alteplase group. The 30-day



**Figure 2.** Differences in the Salvage Index and the Relative Risk of Death, Reinfarction, or Stroke at Six Months in the Stent Group as Compared with the Alteplase Group, According to Various Characteristics.

Horizontal bars indicate the 95 percent confidence intervals.

mortality rate (4.2 percent) did not differ significantly from that of 3.5 percent reported in a recent comparison of stenting with PTCA.<sup>34</sup> In our patients, most of whom had an initial TIMI flow grade of 0 or 1, stenting plus blockade of platelet glycoprotein IIb/IIIa receptors was associated with the full restoration of antegrade blood flow (TIMI grade 3) in 96 percent. This value is 6 percentage points higher than that achieved recently with primary stenting without fibrinogen-receptor blockade.<sup>34</sup> Similar results in favor of abciximab use were also recently reported.<sup>20</sup> In addition, abciximab also substantially improves flow in the microvascular bed,<sup>18</sup> in part because of its antiinflammatory effect of interfering with platelet–leukocyte interactions.<sup>35</sup>

At six months, the clinical results favored the combination of stenting with abciximab. Parallel to the benefit in clinical outcome at six months was the significantly greater degree of myocardial salvage after stenting plus platelet glycoprotein IIb/IIIa blockade in this trial. Although assessing myocardial salvage with <sup>99m</sup>Tc-sestamibi scintigraphy is very attractive, supportive evidence of its value in prognosis from clinical trials with mortality as an end point is still lacking.<sup>28</sup> However, the advantages afforded by increasing the extent of myocardial salvage take time to become clinically apparent, because of the persistence of myocardial stunning with reperfusion therapy.<sup>36</sup> On the basis of our findings, a new reperfusion strategy such as combining stenting with abciximab yields a significantly greater degree of myocardial salvage and a better clinical outcome at six months than does a conventional strategy of fibrinolytic therapy in patients with acute myocardial infarction.

This trial had sufficient statistical power only to assess myocardial salvage. Therefore, the difference

observed in clinical outcome needs to be confirmed by larger trials.

We compared a combined strategy of stenting plus abciximab with alteplase alone; we do not know how much of the benefit can be ascribed to stenting and how much to fibrinogen-receptor blockade. The extent of the benefit appears to be greater than that observed in prior comparisons of tissue plasminogen activator with percutaneous coronary interventions without the adjunctive use of platelet glycoprotein IIb/IIIa blockade for myocardial infarction. Therefore, abciximab may have contributed importantly to our results. The promotion of embolization by either fibrinolytic therapy or catheter-based reperfusion therapy has recently been underscored as a major problem in the treatment of acute myocardial infarction; this problem can largely be surmounted by adjunctive blockade of glycoprotein IIb/IIIa receptors.<sup>37</sup> Our study was designed before the announcement of the results of the TIMI 14 trial, which showed that the addition of abciximab to intravenous therapy with tissue plasminogen activator increased the rate of successful flow restoration.<sup>38</sup> Therefore, further studies are needed to test whether this combined regimen also leads to a greater degree of myocardial salvage than fibrinolytic therapy alone.

Our results were achieved at institutions with high volumes of interventional procedures. Therefore, these results may not be directly applicable to the entire medical community responsible for treating patients with acute myocardial infarction. They may be helpful, nonetheless, in designing future treatment guidelines for these patients.

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## APPENDIX

The following investigators participated in the Stent versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction (STOPAMI) Study: *Steering Committee* — A. Schömig (chairman), M. Schwaiger (cochairman), A. Kastrati, J. Dirschinger, F.-J. Neumann; *Data Coordinating Center* — A. Kastrati, U. Schricke, M. Hadamitzky, H. Kreuzberg; *Scintigraphic Core Laboratory* — U. Schricke, S. Martinoff, J. Neverve, D. Wetzel, S. Nekolla; *Angiographic Core Laboratory* — J. Mehilli, A. Redl, H. Bollwein; *Clinical Follow-up Center* — J. Pache, D. Hall, H. Holle, K. Hösl, K. Stein, F. Albrecht, M. Ibrahim; *Clinical Investigators* — F.-J. Neumann, E. Alt, M. Seyfarth, H. Schühlen, J. Dirschinger, R. Blasini, C. Schmitt, M. Gawaz, N. von Beckerath.

## REFERENCES

- Braunwald E. Myocardial reperfusion, limitation of infarct size, reduction of left ventricular dysfunction, and improved survival: should the paradigm be expanded? *Circulation* 1989;79:441-4.
- Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Long-term effects of intravenous thrombolysis in acute myocardial infarction: final report of the GISSI study. *Lancet* 1987;2:871-4.
- ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;2:349-60.
- Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1993;328:673-9.
- Zijlstra F, de Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. *N Engl J Med* 1993;328:680-4.
- The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. *N Engl J Med* 1997;336:1621-8. [Erratum, *N Engl J Med* 1997;337:287.]
- Zijlstra F, Hoorntje JCA, de Boer M-J, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1999;341:1413-9.
- Nunn CM, O'Neill WW, Rothbaum D, et al. Long-term outcome after primary angioplasty: report from the Primary Angioplasty in Myocardial Infarction (PAMI-I) trial. *J Am Coll Cardiol* 1999;33:640-6.
- Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. *N Engl J Med* 1993;328:685-91.
- Every NR, Parsons LS, Hlatky M, Martin JS, Weaver WD. A comparison of thrombolytic therapy with primary coronary angioplasty for acute myocardial infarction. *N Engl J Med* 1996;335:1253-60.
- Tiefenbrunn AJ, Chandra NC, French WJ, Gore JM, Rogers WJ. Clinical experience with primary percutaneous transluminal coronary angioplasty compared with alteplase (recombinant tissue-type plasminogen activator) in patients with acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMII-2). *J Am Coll Cardiol* 1998;31:1240-5.
- Topol EJ, Van de Werf FJ. Acute myocardial infarction: early diagnosis and management. In: Topol EJ, ed. *Textbook of cardiovascular medicine*. Philadelphia: Lippincott-Raven, 1998:395-435.
- Lincoff AM, Califf RM, Moliterno DJ, et al. Complementary clinical benefits of coronary-artery stenting and blockade of platelet glycoprotein IIb/IIIa receptors. *N Engl J Med* 1999;341:319-27.
- Neumann FJ, Walter H, Richardt G, Schmitt C, Schömig A. Coronary Palmaz-Schatz stent implantation in acute myocardial infarction. *Heart* 1996;75:121-6.
- Schömig A, Neumann FJ, Walter H, et al. Coronary stent placement in patients with acute myocardial infarction: comparison of clinical and angiographic outcome after randomization to antiplatelet or anticoagulant therapy. *J Am Coll Cardiol* 1997;29:28-34.
- Kastrati A, Pache J, Dirschinger J, et al. Primary intracoronary stenting in acute myocardial infarction: long-term clinical and angiographic follow-up and risk factor analysis. *Am Heart J* 2000;139:208-16.
- Brener SJ, Barr LA, Burchenal JEB, et al. Randomized, placebo-controlled trial of platelet glycoprotein IIb/IIIa blockade with primary angioplasty for acute myocardial infarction. *Circulation* 1998;98:734-41.
- Neumann FJ, Blasini R, Schmitt C, et al. Effect of glycoprotein IIb/IIIa receptor blockade on recovery of coronary flow and left ventricular function after the placement of coronary-artery stents in acute myocardial infarction. *Circulation* 1998;98:2695-701.
- The EPISTENT Investigators. Randomised placebo-controlled and balloon-angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein-IIb/IIIa blockade. *Lancet* 1998;352:87-92.
- McGuire DK, Hudson MP, East MA, et al. Highlights from the American Heart Association 72nd Scientific Sessions: November 6 to 10, 1999. *Am Heart J* 2000;139:359-70.
- Schömig A, Neumann F-J, Kastrati A, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. *N Engl J Med* 1996;334:1084-9.
- Nekolla SG, Miethaner C, Nguyen N, Ziegler SI, Schwaiger M. Reproducibility of polar map generation and assessment of defect severity and extent assessment in myocardial perfusion imaging using positron emission tomography. *Eur J Nucl Med* 1998;25:1313-21.
- Gibbons RJ, Verani MS, Behrenbeck T, et al. Feasibility of tomographic <sup>99m</sup>Tc-hexakis-2-methoxy-2-methylpropyl-isonitrile imaging for the assessment of myocardial area at risk and the effect of treatment in acute myocardial infarction. *Circulation* 1989;80:1277-86.
- O'Connor MK, Gibbons RJ, Juni JE, O'Keefe J Jr, Ali A. Quantitative myocardial SPECT for infarct sizing: feasibility of a multicenter trial evaluated using a cardiac phantom. *J Nucl Med* 1995;36:1130-6.
- Elashoff JD. nQuery Advisor version 3.0 user's guide. Cork, Ireland: Statistical Solutions, 1999.
- Okada RD, Glover D, Gaffney T, Williams S. Myocardial kinetics of technetium-99m-hexakis-2-methoxy-2-methylpropyl-isonitrile. *Circulation* 1988;77:491-8.
- Sinusas AJ, Trautman KA, Bergin JD, et al. Quantification of area at risk during coronary occlusion and degree of myocardial salvage after reperfusion with technetium-99m methoxyisobutyl isonitrile. *Circulation* 1990;82:1424-37.
- Gibbons RJ, Miller TD, Christian TF. Infarct size measured by single photon emission computed tomographic imaging with (<sup>99m</sup>Tc)-sestamibi: a measure of the efficacy of therapy in acute myocardial infarction. *Circulation* 2000;101:101-8.
- Gibbons RJ, Christian TF, Hopfenspirger M, Hodge DO, Bailey KR. Myocardium at risk and infarct size after thrombolytic therapy for acute myocardial infarction: implications for the design of randomized trials of acute intervention. *J Am Coll Cardiol* 1994;24:616-23.
- The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993;329:673-82.
- The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. *N Engl J Med* 1997;337:1118-23.
- The Continuous Infusion versus Double-Bolus Administration of Alteplase (COBALT) Investigators. A comparison of continuous infusion of alteplase with double-bolus administration for acute myocardial infarction. *N Engl J Med* 1997;337:1124-30.
- Assessment of the Safety and Efficacy of a New Thrombolytic Investigators. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. *Lancet* 1999;354:716-22.
- Grines CL, Cox DA, Stone GW, et al. Coronary angioplasty with or without stent implantation for acute myocardial infarction. *N Engl J Med* 1999;341:1949-56.
- Neumann FJ, Zohlnhöfer D, Fakhoury L, Ott I, Gawaz M, Schömig A. Effect of glycoprotein IIb/IIIa receptor blockade on platelet-leukocyte interaction and surface expression of the leukocyte integrin Mac-1 in acute myocardial infarction. *J Am Coll Cardiol* 1999;34:1420-6.
- Christian TF, Gitter MJ, Miller TD, Gibbons RJ. Prospective identification of myocardial stunning using technetium-99m sestamibi-based measurements of infarct size. *J Am Coll Cardiol* 1997;30:1633-40.
- Topol EJ, Yadav JS. Recognition of the importance of embolization in atherosclerotic vascular disease. *Circulation* 2000;101:570-80.
- Antman EM, Giugliano RP, Gibson CM, et al. Abciximab facilitates the rate and extent of thrombolysis: results of the Thrombolysis in Myocardial Infarction (TIMI) 14 trial. *Circulation* 1999;99:2720-32.