Glycoprotein IIb/IIIa Receptor Blockade Improves Outcomes in Diabetic Patients Presenting With Unstable Angina/Non–ST-Elevation Myocardial Infarction

Results From the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study

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Background—Diabetic patients who present with unstable angina or non–ST-elevation myocardial infarction suffer a substantially greater incidence of subsequent infarction or death compared with nondiabetic patients. The present study was undertaken to examine whether diabetic patients in the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) study appeared to benefit from platelet glycoprotein IIb/IIIa receptor–mediated inhibition of platelet aggregation by tirofiban.

Methods and Results—Of the 1570 PRISM-PLUS patients treated with either tirofiban plus heparin (n = 773) or heparin alone (n = 797), ≈23% in each treatment group were diabetic. A comparison of treatment outcomes in the diabetic subgroup revealed that the combination therapy compared with heparin alone was associated with reductions in the incidence of the composite primary end point of death, myocardial infarction (MI), or refractory ischemia at 2, 7, 30, and 180 days (7.7% versus 8.3%, 14.8% versus 21.8%, 20.1% versus 29.0%, and 32.0% versus 39.9%, respectively; P = NS) and in the incidence of MI or death (0.0% versus 3.1%, P = 0.03; 1.2% versus 9.3%, P = 0.005; 4.7% versus 15.5%, P = 0.002; and 11.2% versus 19.2%, P = 0.03). Tests for quantitative interaction between tirofiban therapy and diabetic status were significant.

Conclusions—The addition of tirofiban to heparin and aspirin appears effective in the prevention of major ischemic events, particularly MI or death, in diabetic patients presenting with unstable angina and non–ST-elevation MI. (Circulation. 2000;102:2466-2472.)

Key Words: angina ■ myocardial infarction ■ diabetes mellitus ■ glycoproteins ■ tirofiban

Diabetic patients who present with an acute coronary syndrome have an impaired prognosis compared with nondiabetic subjects. Patients with ST-segment elevation myocardial infarction (MI) have a substantially greater incidence of subsequent death or MI.1–4 The presence of diabetes, whether insulin dependent or not, also has a negative impact on the outcome of revascularization procedures.5–7 Such an important negative prognostic factor likely also affects diabetic patients presenting specifically with unstable angina/ non–ST-elevation MI (UA/NSTEMI).8

Recently, in the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial, the addition of antiplatelet therapy with the use of the nonpeptide platelet glycoprotein (GP) IIb/IIIa receptor antagonist tirofiban to standard antithrombotic therapy with heparin and aspirin in patients presenting with UA/NSTEMI was associated with a marked reduction in the rate of ischemic events during the acute phase, with a benefit maintained during a 6-month follow-up.9 Given the poor prognosis associated with diabetes and the possibility that this poor prognosis may be related to platelet hyperactivity as part of a more generalized hypercoagulable state,10,11 it was of interest to determine whether diabetic patients presenting with UA/NSTEMI benefited from inhibition of platelet aggregation with a GP IIb/IIIa receptor antagonist. Interest on the subject has also recently
been expressed in clinical trials of intervention procedures\textsuperscript{12,13} and in accompanying editorial comments.\textsuperscript{14} Therefore, we evaluated, in a post hoc analysis of the PRISM-PLUS data, whether the addition of tirofiban to standard treatment could yield benefit in diabetic patients.

**Methods**

The study population, design, and the main findings of the PRISM-PLUS study are described in detail elsewhere.\textsuperscript{9} The study enrolled 1915 patients with UA/NSTEMI, of whom 23\% were diabetic. Patients were eligible for enrollment if they experienced prolonged anginal pain or repetitive episodes of angina at rest or with minimal exertion in the previous 12 hours accompanied by at least 1 of the following 2 objective measurements: (1) new ST-T wave ischemic changes on the ECG or (2) elevation of plasma levels of creatine kinase (CK) and/or of the CK-MB fraction (CK-MB). Exclusion criteria included ST elevation $>20$ minutes in duration, thrombolysis within the preceding 48 hours, recent PTCA or CABG surgery, a history of stroke within 1 year, active bleeding or high risk of bleeding, angina secondary to identifiable factors, and certain laboratory abnormalities. For the purpose of this analysis, patients were assigned to the diabetic or nondiabetic subgroup on the basis of the presence or absence of a history of diabetes mellitus at study enrollment, as identified by the study investigators in the case report forms, which were all validated by review of the source documents by the study monitors. The study protocol provided no specific definition of diabetes mellitus as a recommended diagnosis.

The double-blind trial randomized patients to 1 of 3 treatment regimens: tirofiban (30-minute loading infusion of 0.6 $\mu$g $\cdot$ kg$^{-1}$ $\cdot$ min$^{-1}$ followed by a maintenance infusion of 0.15 $\mu$g $\cdot$ kg$^{-1}$ $\cdot$ min$^{-1}$) with heparin-placebo, tirofiban (30-minute loading infusion of 0.4 $\mu$g $\cdot$ kg$^{-1}$ $\cdot$ min$^{-1}$ followed by a maintenance infusion of 0.10 $\mu$g $\cdot$ kg$^{-1}$ $\cdot$ min$^{-1}$) with heparin-placebo, or tirofiban-placebo with heparin. Heparin was administered as a bolus of 5000 U followed by 1000 U/h, titrated to achieve an activated partial thromboplastin time that was 2 times control values. The dose was adjusted according to a nomogram by an unblinded coinvestigator or by a central core laboratory. Random adjustments of the heparin-placebo infusion were made to maintain blinding. All patients received 160 to 325 mg QD aspirin starting at the time of randomization.

The study drugs were administered for 48 to 108 hours. Interventions were not allowed during the first 48 hours unless the patient experienced refractory ischemia or a new MI. Between 48 and 96 hours, investigators were encouraged to perform coronary angiography and angioplasty of the culprit lesion, if clinically indicated. In patients undergoing coronary intervention, the heparin or heparin-placebo infusion was discontinued, and a bolus of 5000 to 7500 U of open-label heparin was administered, followed by an infusion at a rate of 1000 U/h, with additional bolus doses as needed. Tirofiban or tirofiban-placebo was continued according to the patient’s study-group assignment through coronary angiography and PTCA and for 12 to 24 hours after the procedure. The infusion of heparin was stopped after the procedure, at least 2 hours before the removal of the sheath.

Randomized patients were followed for 180 days after initiation of the study drug for the occurrence of end points. An independent Data Safety Monitoring Committee reviewed unblinded data at 2 interim analyses. At the first interim efficacy analysis, the tirofiban alone arm of the study was prematurely discontinued on the recommendation of the Data Safety Monitoring Committee because of an excess mortality at 7 days. Therefore, only data from the tirofiban plus heparin group and heparin control arm are presented here.

**Study End Points**

The primary end point of the trial was a composite of death from any cause, new MI, or refractory ischemia within 7 days after randomization. Rehospitalization for UA/NSTEMI was also counted in the composite primary end point when assessed at 7 days, 30 days, and 6 months. Predefined secondary end points included the same composite end point 48 hours and 30 days after randomization, the 3 components of this end point as separate measures, and a composite of death or MI. Other prespecified analyses were outcome among patients in whom a coronary procedure was performed during the initial hospitalization and the frequency of end points at 6 months.

MI was defined as a new episode of chest pain, at least 20 minutes in duration with new Q waves ($>0.03$ second in duration in $\geq 2$ leads), or a rise in the serum CK level to 2 times the upper limit of normal or higher (3 times with infarction related to coronary angioplasty), with elevated CK-MB values. CK measurements were routinely obtained before randomization and after 24 and 48 hours. Additional measurements were performed when the patients experienced an episode of ischemic chest pain lasting $\geq 10$ minutes inclusive of episodes occurring per cardiac catheterization; these measurements were repeated on a 6- to 8-hour interval for 24 hours. No routine determinations were performed after reperfusion procedures. If an evolving infarction was present at study entry, a new increase in CK and CK-MB levels to $>50\%$ above the previous value after an initial peak was required. A perioperative MI was defined by new Q waves. Refractory ischemic conditions included the following 3 sets of signs and symptoms: chest pain $\geq 20$ minutes in duration or 2 episodes of chest pain (each lasting $\geq 10$ minutes) within a 1-hour period, with transient ST-T changes while the patient was receiving medical therapy adjusted to heart rate and blood pressure; recurrent ischemia with pulmonary edema or hypotension; or refractory chest pain ($\geq 3$ episodes, each $\geq 5$ minutes in duration) necessitating intra-aortic counterpulsation or urgent intervention within 12 hours. All events were evaluated by an end-point committee whose members were blinded to treatment assignments. Adjudication required the agreement of 2 independent evaluators. When these 2 disagreed, a third reviewer also evaluated the data, and consensus was sought. If consensus could not be reached, the evaluation by the chairman of the committee was used in the analysis.

**Assessment of Safety**

Bleeding events were assessed throughout the period of study drug infusion and for 24 hours after infusion by using the criteria developed by the Thrombolysis in Myocardial Infarction (TIMI) trial group. Major bleeding was defined as a decrease in the hemoglobin levels of 50 g/L or cardiac tamponade, and minor bleeding was defined as a decrease of $>30$ g/L.\textsuperscript{15}

**Statistical Analysis**

As for the main trial, the comparisons were limited to patients randomized to the tirofiban plus heparin and heparin arms, excluding the tirofiban alone arm because of a lack of statistical power by premature discontinuation. Baseline characteristics between diabetic and nondiabetic patients were compared by $t$ test and $\chi^2$ test. The significance of differences between groups was assessed by a Cox regression analysis\textsuperscript{16} implemented by the SAS PHREG procedure (SAS Institute); the risk ratios (or hazard ratios) presented are based on this model. To account for a possible baseline imbalance in risk between the treatment groups, additional Cox regression analyses were performed with a 4-point risk score as a covariate. This score represented the mathematical sum of the baseline variables independently associated by multiple logistic regression with a higher incidence of end-point events in the PRISM-PLUS population. These independent predictors were age, prior CABG, prior aspirin use, prior $\beta$-blocker use, and ST-segment depression on presentation. The score assigned patients was 1 point for each predictor present, because the odds for an adverse event were approximately the same. Tests for interaction between tirofiban therapy and diabetic status were also based on the Cox regression analysis model with use of the likelihood ratio test. This is a test to determine whether the effect of tirofiban is similar among diabetic and nondiabetic patients. An intention-to-treat analysis was performed, excluding no randomized patients.
Results

Patient Characteristics

A total of 1570 patients were enrolled into the tirofiban plus heparin (n=773) or heparin alone (n=797) arms of the PRISM-PLUS study. Of these patients, 21.9% of the tirofiban plus heparin patients (n=169) and 24.2% of the heparin patients (n=193) were identified as diabetics. Table 1 describes the demographic characteristics of diabetic and non-diabetic subpopulations of the PRISM-PLUS study. Overall, compared with nondiabetic patients, diabetic patients tended to have a greater incidence of prior coronary artery disease and prior coronary artery procedures, hypertension, hypercholesterolemia, and ST-segment depression. Within the diabetic population, the subgroups of patients who received tirofiban plus heparin or heparin alone were well matched regarding baseline characteristics and angiographic findings, with the exceptions being a greater incidence of prior CABG and smoking in the tirofiban plus heparin arm and more frequent ST-segment depression and use of oral antidiabetic agents in the heparin alone arm.

Treatment strategies used during initial hospitalization did not vary appreciably by diabetic status. The duration of study drug infusion was comparable between diabetic and nondiabetic patient subgroups, at 69.7 ± 22.3 and 72.1 ± 19.7 hours, respectively. Diabetic and nondiabetic subgroups were also similar with respect to invasive procedures undertaken; the percentages of patients undergoing a percutaneous coronary intervention (PCI) in the diabetic and nondiabetic subgroups were 29.6% and 32.6%, respectively (P=NS), and the per-

<table>
<thead>
<tr>
<th>TABLE 1. Baseline Characteristics of Patient Population</th>
<th>Heparin</th>
<th>Tirofiban+Heparin</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Characteristics</td>
<td>DM (n=193)</td>
<td>No DM (n=604)</td>
<td>DM (n=169)</td>
</tr>
<tr>
<td>Age, y (mean±SD)</td>
<td>66±9.8</td>
<td>62±11.9</td>
<td>65±10.2</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61</td>
<td>71</td>
<td>66</td>
</tr>
<tr>
<td>Female</td>
<td>39</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>Previous coronary disease and procedures, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>67</td>
<td>53</td>
<td>69</td>
</tr>
<tr>
<td>MI</td>
<td>44</td>
<td>37</td>
<td>50</td>
</tr>
<tr>
<td>Heart failure</td>
<td>16</td>
<td>6.0</td>
<td>17</td>
</tr>
<tr>
<td>PCI</td>
<td>12</td>
<td>8.4</td>
<td>10</td>
</tr>
<tr>
<td>CABG</td>
<td>15</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>Risk factors, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>21</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73</td>
<td>50</td>
<td>71</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>55</td>
<td>48</td>
<td>57</td>
</tr>
<tr>
<td>Diagnosis, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>59</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>Non-ST-elevation MI</td>
<td>41</td>
<td>48</td>
<td>42</td>
</tr>
<tr>
<td>Evidence of ischemia, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td>9.9</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>ST-segment depression</td>
<td>72</td>
<td>57</td>
<td>60</td>
</tr>
<tr>
<td>T-wave inversion</td>
<td>47</td>
<td>54</td>
<td>52</td>
</tr>
<tr>
<td>Prior therapy, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>89</td>
<td>87</td>
<td>88</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>57</td>
<td>52</td>
<td>61</td>
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<tr>
<td>Calcium channel blocker</td>
<td>50</td>
<td>35</td>
<td>53</td>
</tr>
<tr>
<td>Insulin</td>
<td>27</td>
<td>0.0</td>
<td>27</td>
</tr>
<tr>
<td>Oral antidiabetic agent</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sulfonylurea</td>
<td>45</td>
<td>0.0</td>
<td>45</td>
</tr>
<tr>
<td>Antihyperglycemic agent*</td>
<td>25</td>
<td>0.2</td>
<td>17</td>
</tr>
<tr>
<td>Sulfonylurea/antihyperglycemic</td>
<td>53</td>
<td>0.2</td>
<td>49</td>
</tr>
<tr>
<td>No diabetes medications</td>
<td>26</td>
<td>99.8</td>
<td>31</td>
</tr>
</tbody>
</table>

DM indicates diabetes mellitus; n, number of patients.

*Biguanides, l-glucosidase inhibitors, and insulin sensitizers (thiazolidinediones).
percentages undergoing surgery were 24.3% and 22.9%, respectively ($P > 0.05$). However, diabetic patients had a greater incidence of 2- or 3-vessel coronary artery disease on angiography than did nondiabetic patients (74% versus 63%, respectively; $P < 0.001$).

Incidence of Cardiac Ischemic Events
The incidences of the composite primary end point of death, MI, refractory ischemia, and readmission for UA/NSTEMI and the incidences of the combined end point of MI and death in diabetic versus nondiabetic patients irrespective of treatment group are presented in Table 2. Diabetic patients tended to experience a greater incidence of the composite primary end point than did nondiabetic patients at all time points. This increased incidence of adverse cardiac events was evident as early as 48 hours after presentation, was still apparent at 180 days, and was mainly driven by a greater incidence of refractory ischemic conditions, although the rate of MI and death was also higher at late follow-up.

The incidences of the composite primary end point and of the combined end point of MI and death in diabetic and nondiabetic patients by treatment allocation are presented in Figure 1. At all time points, there was a nonstatistically significant lower incidence of the composite primary end point in patients who received tirofiban (Figure 2). However, there was a significant reduction in the rate of MI or death (Figure 3). There were 2 deaths and no MIs at 7 days in diabetic patients who received tirofiban plus heparin for an incidence of the combined end point of MI and death of 1.2%. In contrast, the incidence of MI and death at this time point in diabetic patients who received heparin alone was 9.3% ($P < 0.005$), a rate comparable to that observed in nondiabetic patients. The reduction in the incidence of MI and death was durable. Thus, the absolute reductions between the patient subgroups who received tirofiban plus heparin or heparin alone were 8.1%, 10.8%, and 8.0% at 7, 30, and 180 days, respectively.

In patients with ST-segment depression at baseline, the risk of MI or death at 30 days was reduced from 16.7% (23 of 138 patients) to 6.9% (7 of 102 patients), and in patients with no ST depression, the risk was reduced from 12.7% (7 of 55 patients) to 1.5% (1 of 67 patients). The calculated risk scores

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### TABLE 2. Outcomes at 2, 7, 30, and 180 Days: Diabetics vs Nondiabetics

<table>
<thead>
<tr>
<th>Time and Event</th>
<th>Nondiabetics (n=1208), n (%)</th>
<th>Diabetics (n=362), n (%)</th>
<th>Risk Ratio (CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>24 (2.0)</td>
<td>176 (48.9)</td>
<td>1.76 (1.20–2.60)</td>
<td>0.005</td>
</tr>
<tr>
<td>MI/Death</td>
<td>16 (1.3)</td>
<td>164 (45.3)</td>
<td>2.54 (1.50–4.33)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

* Statistically significant ($P < 0.05$) interactions were found between tirofiban therapy and diabetic status for these endpoints, suggesting that tirofiban was more efficacious among diabetic than among non-diabetic patients.

* Not defined.
based on baseline characteristics were similarly distributed among the 2 treatment groups. Covariate adjustment for the score at baseline had no influence on the results. Thus, the relative risk for the 30-day MI/death end point was 0.283 (P = 0.0015) without an adjustment and 0.290 (P = 0.0019) after the adjustment.

The specific antidiabetic therapy used did not appear to influence the results seen with the addition of tirofiban, although the wide interval confidences around the relative risks preclude firm interpretation. At 30 days, the risk reduction for the composite end point was 3% in patients receiving insulin, 33% in those receiving an oral hypoglycemic, and 48% in patients receiving no therapy; risk reductions for the end point of MI or death were 73%, 58%, and 87%, respectively.

Figure 4 shows stratification by treatment strategy of efficacy outcomes 30 days after randomization in diabetic patients by treatment orientation in hospital. The trends in risk reduction were in the same direction whether patients underwent PCI, CABG, or no revascularization; it was greater in patients undergoing an intervention procedure, including coronary artery bypass surgery, but with overlapping CIs.

Statistical tests for quantitative interaction between tirofiban therapy and diabetic status were significant, indicating that the effect of tirofiban was quantitatively even stronger among diabetic than among nondiabetic patients in reducing the incidence of MI/death (although not the composite), particularly at 7 and at 30 days (P = 0.061 for MI/death and P = 0.37 for triple composite at 2 days, P = 0.006 for MI/death and P = 0.93 for composite at 7 days, P = 0.007 for MI/death and P = 0.41 for composite at 30 days, and P = 0.16 for MI/death and P = 0.60 for composite at 180 days).

**Bleeding Complications**

The incidence of bleeding complications in patients who received tirofiban plus heparin or heparin alone, stratified by diabetic status, is presented in Table 3. There was a modest though not statistically significant incremental risk of bleeding with the combination of tirofiban plus heparin. Compared with nondiabetic patients, diabetic patients as a group had a somewhat lower incidence of major and minor bleeding events and minimal excess with the addition of tirofiban to heparin.

**Discussion**

Diabetes mellitus is present in a significant percentage of patients hospitalized with acute coronary syndromes and profoundly affects the biology of cardiovascular disease. For example, it has been shown that platelets from diabetic patients are hyperresponsive to platelet agonists and that circulating platelets are activated. In both UA/NSTEMI and PCI settings, compared with nondiabetic patients, insulin-dependent and non–insulin-dependent diabetic patients experience a higher mortality during the acute phase of MI, followed by a greater morbidity afterward. In the Global Utilization of Streptokinase and tPA for Occluded Arteries (GUSTO)-I angiography substudy report revealed a 2-fold increase in relative risk of 30-day mortality among diabetic patients relative to nondiabetic patients. Diabetic patients also have an increased morbidity and mortality after PCI, perhaps because of a higher incidence of complex plaque morphology and predisposition for atherosclerotic plaque rupture and intraluminal thrombosis. Van
Belle et al. have shown that unstable plaques may remain active with thrombus for ≥30 days after the responsible index coronary event despite therapy with thrombolytics, such that the early advantages of lytic agents may be lost if the underlying unstable plaque is not passivated by PCI or GP IIb/IIIa receptor antagonists.

Given the poor prognosis associated with diabetes and the possibility that this poor prognosis may be related to platelet hyperactivity as part of a more generalized hypercoagulable state, we undertook substudy analysis to examine whether diabetic patients presenting with UA/NSTEMI appeared to benefit as much as did nondiabetic patients from inhibition of platelet aggregation mediated by tirofiban. Our results indicate that tirofiban in combination with heparin and aspirin reduced the incidence of the composite primary end point similarly in diabetic patients presenting with UA/NSTEMI and in nondiabetic patients. The benefit of tirofiban consisted mainly in prevention of MI or death and was present with medical management as well as with PCI and CABG. This finding extends to UA/NSTEMI the benefit of GP IIb/IIIa blockade observed in PCI trials. In the Evaluation of Platelet IIb/IIIa Inhibitor for Stenting (EPISTENT) trial, abciximab reduced the 6-month rate of death or MI in patients randomized to balloon angioplasty as well as to stent implantation; the rate of target vessel revascularization was reduced only in the abciximab plus stent group. A meta-analysis of 3 PCI trials showed a significant reduction in the mortality rates at 12 months with abciximab used at the time of procedures.

Study Limitations

Retrospective subgroup analyses have inherent limitations that should be acknowledged as they relate to the present study. First, our analysis based on diabetic status is post hoc. Although diabetic patients were identified as a prespecified subgroup for analysis, diabetic status was not used to stratify patients at randomization. PRISM-PLUS was not designed to characterize the effects of tirofiban in diabetic patients and was not powered to document a special benefit in these patients. Second, because the number of patients within the diabetic cohort was small, the CIs for the effect of tirofiban in this cohort were wide. Third, in the analysis of 30-day outcomes in diabetic patients by revascularization strategy, the selection of revascularization strategy during the initial hospitalization was made by the clinical investigators and therefore influenced by treatment assignment. Therefore, the data need to be interpreted with caution as suggestive rather than definitive. Nevertheless, the results observed in the present study, with an 89% reduction in the risk of death/MI at 7 days (absolute reduction 8.1%) and a 70% reduction at 30 days (absolute reduction 10.8%), are substantial. These observations, along with those of the PCI trials, suggest a potential benefit of GP IIb/IIIa antagonists in diabetic patients, one that deserves further research. Such research may lead to the improved clinical management of diabetic patients and to a better understanding of the mechanisms that impair prognosis in these patients.

Clinical Implications

The present study suggests that treatment with tirofiban may be of benefit in diabetic patients by preventing the ischemic complications of acute coronary syndromes. The benefit was present in patients managed medically and was of greater magnitude in the setting of revascularization procedures (PCI and CABG), which are known to be associated with increased morbidity and mortality in diabetic patients. Events prevented were mainly death and MI, with the reduction being more marked than in nondiabetic patients and with a significant interaction observed between diabetic status and the administration of tirofiban. The reasons for this greater effect on death and MI are not clear and could be related to the relatively small number of events. However, they may be related to some pathophysiological mechanism present in diabetic patients that causes more potent thrombogenic stimulation and MI and that is responsive to GP IIb/IIIa antagonist therapy.

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