Prehospital Therapy With the Platelet Glycoprotein IIb/IIIa Inhibitor Eptifibatide in Patients With Suspected Acute Coronary Syndromes* The Bochum Feasibility Study

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Study objectives: To assess the practical application and safety of prehospital antithrombotic therapy with the glycoprotein (GP) IIb/IIIa inhibitor eptifibatide for patients with suspected acute coronary syndrome (ACS) or myocardial infarction (MI).

Design: Open-labeled pilot study. Patients with typical chest pain who were seen within 6 h of the onset of symptoms were enrolled in the mobile emergency ambulance. Patients were stratified by even/uneven days to receive standard treatment or standard treatment plus an IV bolus of eptifibatide (180 μg/kg body weight) followed by a continuous eptifibatide infusion (2 μg/kg/min). The main outcome measurement was a combination of prehospital or in-hospital death, reinfarction, revascularization of target vessels, and major bleeding complications.

Results: A total of 356 patients (age range, 29 to 75 years; women, 24.7%) were included in the analysis. On admission to the hospital, the diagnosis of ACS or MI was confirmed in approximately 60% of patients, and alternative diagnoses were made in 40% of patients. The rates of complications, including fatal and nonfatal complications occurring during transportation and during subsequent hospitalization, were similar in both study groups. The primary end point occurred in 11.8% of patients in the control group, and in 9.6% of those in the eptifibatide group (difference not significant).

Conclusion: The prehospital administration of the GP IIb/IIIa inhibitor eptifibatide is feasible and safe in patients with clinically suspected ACS and MI. The benefit of this treatment has yet to be established in a large-scale multicenter study.

Key words: acute coronary syndrome; eptifibatide; glycoprotein IIb/IIIa inhibitor; myocardial infarction; primary percutaneous coronary intervention

Abbreviations: ACS = acute coronary syndrome; CAD = coronary artery disease; CK = creatinine kinase; GP = glycoprotein inhibitor; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; TIMI = thrombolysis in myocardial infarction; UA = unstable angina

A cute coronary syndromes (ACSs) are characterized by an imbalance between myocardial oxygen supply and demand, which is commonly caused by a reduced coronary blood flow. Unstable angina (UA) is differentiated from non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI) according to the release of biochemical markers of myocardial necrosis and/or ST-segment elevations seen in the surface ECG.¹,² This differentiation is part of an evidence-based risk stratification that is used to target more aggressive antithrombotic and interventional therapies in patients presenting with ACS and STEMI. The over-riding principles for treatment of patients with STEMI and ACS are the achievement of infarct-related artery patency and ruptured plaque stabilization.¹,² Keeping the time delay between the onset of symptoms and the initiation of an adequate therapy as short as possible is equally important.

Until now, the strategies for reducing time delays have mainly focused on prehospital management.³ Prehospital management encompasses community planning, public awareness, prehospital diagnosis, and prehospital therapy.³ All of these factors are aimed at facilitating and accelerating diagnostic procedures and therapeutic consequences once the
hospital is reached. Several trials have addressed the safety and usefulness of prehospital thrombolysis in patients with STEMI, and have shown reductions in both time to treatment and in mortality, especially in rural areas. No specific prehospital management plan has yet been defined for patients with ACS. These patients are admitted to hospital emergency departments more frequently than are patients with STEMI.

Guidelines for the in-hospital management of patients with ACS and STEMI have addressed the superior role of early percutaneous coronary interventions (PCIs), particularly in combination with glycoprotein (GP) IIb/IIIa inhibitors. In the Abciximab Before Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long-term Follow-up trial, the additional application of the GP IIb/IIIa inhibitor abciximab before acute PCI/stenting in patients with STEMI already had improved coronary patency prior to stenting, the success rate of the stenting procedure, as well as the rate of coronary patency and clinical outcome at 6 months. For patients with non-ST-elevation ACS, a meta-analysis of randomized trials revealed a benefit for early PCIs. The benefit was more pronounced if the procedure was performed while a GP IIb/IIIa inhibitor was being infused.

In the present pilot study, we addressed the feasibility of prehospital antithrombotic treatment for patients with suspected ACS and myocardial infarction (MI). For our purposes, we chose the GP IIb/IIIa inhibitor eptifibatide for antithrombotic treatment since it inhibits platelet aggregation most consistently. A second rationale for the use of a GP IIb/IIIa inhibitor was the fact that this type of comedication improves the success rate and outcome in high-risk patients undergoing PCI. This form of therapy is being used increasingly as the primary treatment in patients presenting with ACS and STEMI. A third rationale, derived from past experiences, was that a definitive diagnosis of ACS, and frequently of MI as well, is difficult or even impossible to achieve in the setting of mobile emergency ambulances. The potential side effects of GP IIb/IIIa inhibitors under these circumstances appear to be tenable in patients with suspected but not proven ACS or STEMI.

Materials and Methods

Patients

Patients were enrolled into the study by emergency medical personnel outside the hospital setting. Patients with pain that was characteristic of MI/ACS who were seen within 6 h of the onset of symptoms were eligible for inclusion in the study. Patients were excluded if they were <18 years of age or >75 years of age, if they were receiving oral phenprocoumon (Marcumar; CT-Arzneimittel; Berlin, Germany) treatment, if they were known to have a hemorrhagic diathesis, or if they had recently (i.e., <4 weeks) received a diagnosis of active peptic ulcer disease, had experienced a stroke, surgery or major trauma within the preceding 3 months, if they were known or suspected to be pregnant, and if they declined to give their informal consent to participate. They also could be excluded from the study for other reasons at the discretion of the emergency medical doctor.

Prehospital treatment was started at a patient’s home or in the mobile ambulance unit. The decision to classify a patient’s symptom as suspected ACS or MI was made by the emergency medical doctor. Since at the time of this study the emergency ambulance vehicles were equipped only with a one-channel ECG recording system, classification of ACS/MI could not be based exclusively on ECG readings. As a general rule, the emergency ambulance team would transfer a patient to the nearest hospital, but they could also transfer the patient to a hospital equipped with a catheterization laboratory providing a 24-h on-call service for acute PCI. The average time taken to transfer a patient from home to the nearest hospital by ambulance was usually <15 min. The emergency doctors are recruited from the divisions of internal medicine, surgery, and anesthesiology.

Three mobile rescue ambulances covering Bochum City (population, approximately 400,000) participated. Three hospitals were equipped with a cardiac catheterization laboratory. In two of the hospitals, a 24-h on-call duty for acute PCI also existed. The routine annual PCI volume of these two units exceeds 400 and 700 interventions. The time period from home to treatment with emergency PCI in patients with STEMI is <60 min.

Study Design

Patients were enrolled in an open-labeled study that was conducted by the Department of Cardiology & Angiology at the Ruhr-University Bochum in cooperation with the Bochum City Fire Department, which is in charge of the mobile ambulances. The study consisted of the following two parts: 0 to 3 months; and 4 to 15 months (i.e., April 1, 2001 to June 30, 2002). During the first 3 months, only control patients receiving standard prehospital treatment in the mobile emergency units were enrolled. The first 3 months were used to establish a data collection procedure.
and to define the participating hospitals. During the following 12 months, patients were stratified according to even and uneven calendar days, and received either standard treatment on even days (ie, the control group) or standard treatment plus eptifibatide on uneven days (ie, the eptifibatide group). The protocol was approved by the institutional review board at the Ruhr-University Bochum. A patient’s informed consent was obtained in the mobile emergency ambulance. A second consent was obtained from the patient by medical hospital staff a day after hospital admission. The second written consent included a record of the patient’s statistical data.

The standard treatment for patients with suspected ACS/MI in the mobile emergency ambulance consisted of IV aspirin (500 mg; Aspisol; Bayer AG; Leverkusen Germany), oral nitrates, and fluids. Other medications (eg, heparin, sedatives, catecholamines, and morphine) were administered by the emergency medical doctor as required. Eptifibatide was administered in addition to the standard treatment as an IV bolus (180 μg/kg body weight) followed by a continuous infusion (2 μg/kg/min). The three emergency ambulances were equipped with a small refrigerator to store eptifibatide at 8°C.

On arrival at the hospital, hospital staff could start, continue, or stop treatment with eptifibatide, initiate thrombolysis, or transfer the patient for emergency PCI. We did not attempt to standardize prehospital or hospital care beyond common practice, therefore, the care provided remained fully representative of the locally established treatment plans.

In order to define STEMI and ACS according to the Braunwald classification, and to actualize the treatment strategies in these patients, all emergency doctors, irrespective of their subspecialty, were required to attend a 2-h training seminar at the beginning of this study. The seminar, which was conducted by a cardiologist, also placed emphasis on the benefit of treatment with primary PCI in patients with troponin-positive ACS and STEMI over that with conventional thrombolysis.

Data Collection, End Points, and Statistical Analysis

Report forms from the emergency ambulance transfer as well as the patient’s hospital charts were analyzed. Data analysis included ECG readings and laboratory findings at the time of hospital admission, as well as diagnosis, therapy, bleeding complications, and outcome since the time of hospital admission. Major bleeding was defined as intracerebral bleeding, a decrease in hemoglobin of > 3 g/dL, as well as a hemorrhage requiring surgery or transfusion. Since the normal ranges of laboratory parameters varied slightly between participating hospitals, the abnormal values reported in the present study are in accordance with the local reference ranges.

The primary end point of this pilot study was a combination of prehospital or in-hospital death, reinfarction, revascularization of the target vessels, and major bleeding complications. Reinfarction was defined according to clinical symptoms and new ECG changes with a new elevation of serum creatinine kinase (CK) levels. Revascularization was defined as a repeat PCI procedure or coronary artery bypass grafting on the primary reperfused target vessel. The secondary end points were the baseline thrombolysis in myocardial infarction (TIMI) flow grade before the patient underwent emergency PCI, the peak CK-myocardial bound level, and the frequency of congestive heart failure/shock and major bleeding complications. The TIMI flow grade (ie, none, minimal, partial, or complete perfusion) was graded retrospectively by two invasive cardiologists who were blinded to the patient’s prehospital treatment.

The data evaluated in this study include categoric, ordered categoric, and continuous variables. Categoric variables are presented as frequencies (ie, as percentages of patients with the characteristics). Continuous measurements are presented as the mean with SD. The χ² test was used to evaluate associations between nonordered categoric variables. For dichotomous variables, the p value from the Fisher exact test result is provided in situations in which expected cell frequencies were too low to use the χ² test. The Wilcoxon rank sum test was used for ordered categoric and continuous variables. A p value of < 0.05 was considered to be statistically significant. The control patients during the first 3 months and during the allocation period were pooled.

Results

Prehospital Diagnosis, Therapy, and Complications

A total of 422 patients with suspected ACS/MI were screened in this study. Fifty-one patients were excluded from the study because they were > 75 years of age (eptifibatide group, 19 patients; control group, 32 patients). Four patients were excluded from the study because of known contraindications for GP IIb/IIIa inhibitors (current phenprocoumon treatment, three patients; known angiodysplasia, one patient). Eleven patients were excluded from the analysis because of missing data (eptifibatide group, 4 patients; control group, 7 patients). Table 1 sum-

Table 1—Demographic Data, Prehospital Diagnosis, Therapy, and Complications*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group</th>
<th>Eptifibatide Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
<td>221</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>Months 0–3</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months 4–15 (randomization)</td>
<td>148</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td>64.1 ± 11.2</td>
<td>65.5 ± 11.7</td>
<td>NS</td>
</tr>
<tr>
<td>Female gender, No.</td>
<td>54 (24.4)</td>
<td>34 (25.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Suspected diagnosis</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>58.9</td>
<td>54.3</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>41.1</td>
<td>45.7</td>
<td></td>
</tr>
<tr>
<td>CAD history</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Known CAD</td>
<td>22.7</td>
<td>20.7</td>
<td></td>
</tr>
<tr>
<td>Known diabetes mellitus</td>
<td>7.6</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>Known CAD + diabetes</td>
<td>16.2</td>
<td>17.2</td>
<td></td>
</tr>
<tr>
<td>No CAD/diabetes</td>
<td>53.5</td>
<td>55.2</td>
<td></td>
</tr>
<tr>
<td>Prehospital therapy</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Aspirin</td>
<td>90.1</td>
<td>90.2</td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>41.1</td>
<td>37.9</td>
<td></td>
</tr>
<tr>
<td>Nitrates/B-blocker</td>
<td>61.1</td>
<td>62.1</td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td>4.8</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Volume substitution</td>
<td>77.3</td>
<td>78.7</td>
<td></td>
</tr>
<tr>
<td>Analgesia</td>
<td>38.6</td>
<td>41.6</td>
<td></td>
</tr>
<tr>
<td>Catecholamines</td>
<td>3.2</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Prehospital complications</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Any complication, No.</td>
<td>19 (8.6)</td>
<td>10 (7.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Ventricular</td>
<td>4.1</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>fibrillation/resuscitation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>0.4</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>4.1</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Values given as mean ± SD or %, unless otherwise indicated. Values in parentheses are %. NS = not significant.
Hospital Diagnosis, Therapy, and Outcome

At the time of admission to the hospital, STEMI was diagnosed in 30.3% of the control group and in 34.1% of the eptifibatide group (Table 2). An ACS (US/NSTEMI) was diagnosed in 25.8% of the control group and in 25.9% of the eptifibatide. Approximately 60% of patients with ACS had a positive troponin (either I or T) test result. All in all, 81 patients (60%) who had been assigned to the eptifibatide group and 124 patients (56.1%) in the control group had a definite diagnosis of ACS or STEMI. In the remaining patients, alternative diagnoses to ACS or STEMI were made in the hospital (Table 2). After excluding STEMI/ACS or establishing an alternative diagnosis, the infusion with eptifibatide was stopped immediately.

Treatment with GP IIb/IIIa inhibitors was continued in the vast majority of patients with STEMI or ACS who had started receiving eptifibatide therapy before being admitted to the hospital (97.5%). In contrast, a new therapy with GP IIb/IIIa inhibitors was started in only 39.5% of the patients in the control group (p < 0.01) [Table 3].

Seventy-seven patients (95.1%) in the eptifibatide group and 101 patients (81.5%) in the control group underwent cardiac catheterization within 2 h of hospital admission. The percentage of patients with ACS/STEMI undergoing coronary angiography was significantly higher in the eptifibatide group than in the control group (95.1% vs 81.5%, respectively; p < 0.01). The vast majority of patients underwent primary PCI (Table 3).

Table 2—Clinical Diagnosis After Hospital Admission*

<table>
<thead>
<tr>
<th>Hospital diagnosis</th>
<th>Control Group (n = 221)</th>
<th>Eptifibatide Group (n = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI</td>
<td>67 (30.3)</td>
<td>46 (34.1)</td>
</tr>
<tr>
<td>US/NSTEMI</td>
<td>57 (25.8)</td>
<td>35 (25.9)</td>
</tr>
<tr>
<td>Troponin† positive</td>
<td>35 (15.8)</td>
<td>23 (17.0)</td>
</tr>
<tr>
<td>Non-ACS/STEMI chest pain</td>
<td>97 (43.9)</td>
<td>54 (40.0)</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>13 (6.0)</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Malignant hypertension</td>
<td>14 (6.3)</td>
<td>7 (5.2)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2 (0.9)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Acute pericarditis/myocarditis</td>
<td>1 (0.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>End-stage heart failure</td>
<td>4 (1.8)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>GI disorders</td>
<td>20 (9.0)</td>
<td>15 (11.1)</td>
</tr>
<tr>
<td>Vertebral disorders</td>
<td>9 (4.0)</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Others</td>
<td>33 (15.0)</td>
<td>19 (14.2)</td>
</tr>
</tbody>
</table>

*p Values given as No. (%).
†Troponin T or troponin I.

Table 3—Hospital Therapy in Patients With ACS/STEMI

<table>
<thead>
<tr>
<th>Hospital Therapy</th>
<th>Control Group (n = 124)</th>
<th>Eptifibatide Group (n = 81)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP IIb/IIIa</td>
<td>49 (39.5)</td>
<td>79 (97.5)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>inhibitor†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>11</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Tirofiban</td>
<td>25</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Abciximab</td>
<td>13</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>5 (4.0)</td>
<td>2 (2.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary</td>
<td>101 (81.5)</td>
<td>77 (95.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>angiography†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute PCI</td>
<td>84 (67.7)</td>
<td>59 (72.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Success rate‡</td>
<td>76 (90.4)</td>
<td>54 (91.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Urgent CABG</td>
<td>2 (1.6)</td>
<td>1 (1.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Target vessel (judged from catheter study)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>LAD</td>
<td>44 (34.6)</td>
<td>29 (37.7)</td>
<td></td>
</tr>
<tr>
<td>Cx</td>
<td>14 (13.8)</td>
<td>12 (15.6)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>25 (24.8)</td>
<td>21 (27.2)</td>
<td></td>
</tr>
<tr>
<td>Graft</td>
<td>2 (2.0)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>LMCA</td>
<td>0 (0)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Not identified]</td>
<td>16 (15.8)</td>
<td>13 (16.9)</td>
<td></td>
</tr>
<tr>
<td>Baseline TIMI flow grade</td>
<td></td>
<td></td>
<td>0.020</td>
</tr>
<tr>
<td>0</td>
<td>38 (37.6)</td>
<td>21 (27.2)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16 (15.8)</td>
<td>6 (7.8)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>9 (8.9)</td>
<td>20 (26.0)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>36 (35.6)</td>
<td>29 (37.6)</td>
<td></td>
</tr>
<tr>
<td>Not classified]</td>
<td>2 (2.0)</td>
<td>1 (1.3)</td>
<td></td>
</tr>
<tr>
<td>Peak CK-MB level, U/L</td>
<td>61.9 ± 65.8</td>
<td>57.6 ± 66.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

*p Values given as No. (%) or mean ± SD, unless otherwise indicated.
†CABG = coronary artery bypass grafting; LAD = left anterior descending artery; Cx = circumflex artery; RCA = right coronary artery; LMCA = left main stem; MB = myocardial bound. See Table 1 for abbreviation not used in the text.
‡For the control group, therapy with GP IIb/IIIa inhibitors was initiated. For the eptifibatide group, therapy with GP IIb/IIIa inhibitors could be continued, stopped, or changed.
§Within 2 h after hospital admission.
¶Identification of culprit lesion/TIMI flow grade not possible because several vessels were closed/severely diseased or only minor diseased arteries were present.

†Troponin T or troponin I.
According to the coronary angiogram findings, a culprit lesion could be identified in > 80% of the patients in both the control group and the eptifibatide group (Table 3). The filling and clearance of the contrast medium (ie, TIMI flow) preceding any intervention was on average more rapid in patients receiving eptifibatide (Table 3). However, while in the hospital the peak CK-myocardial bound levels did not differ between the study groups (Table 3).

Seven patients (3.2%) in the control group and four patients (3.0%) in the eptifibatide group died while in the hospital (Table 4). Nonfatal complications occurred in 22.6% of the control patients and in 17.8% of the patients in the eptifibatide group. Major bleeding complications were observed in both groups with a comparable frequency. The occurrence of the primary composite end point (a combination of prehospital and in-hospital death, reinfarction, repeat PCI/coronary artery bypass grafting of the target vessel, and major bleeding complication) showed no significant difference between the groups (control group, 11.8%; eptifibatide group, 9.6%; p = 0.53) [Table 4]. In a subgroup analysis considering only those patients who had ACS/STEMI, 5 of 124 patients (4.0%) in the control group and 3 of 81 patients (3.7%) in the eptifibatide group died while in the hospital (difference not significant). The incidence of the primary composite end point was not different between the groups (control group, 13.7%; eptifibatide group, 12.3%; p = 0.77).

**Table 4—In-Hospital Complications/Events***

<table>
<thead>
<tr>
<th>Events</th>
<th>Control Group</th>
<th>Eptifibatide Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>164 (74.2)</td>
<td>107 (79.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>7 (3.2)</td>
<td>4 (3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Cerebral hypoxia after CPR</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>0 (0)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>3 (1.4)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Rupture of the left ventricle</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Nonfatal complications</td>
<td>50 (22.6)</td>
<td>24 (17.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>21 (9.5)</td>
<td>11 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>17 (7.7)</td>
<td>9 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>4 (1.8)</td>
<td>2 (1.5)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>6 (2.7)</td>
<td>5 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Repeat PCI</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Reinfarction</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>4 (1.8)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure/</td>
<td>14 (6.3)</td>
<td>6 (4.4)</td>
<td></td>
</tr>
<tr>
<td>NYHA grade &gt; III</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral hypoxia</td>
<td>3 (1.4)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Primary composite end point, n (%)</td>
<td>26 (11.8)</td>
<td>13 (9.6)</td>
<td>NS</td>
</tr>
</tbody>
</table>

***Values given as No. (%), unless otherwise indicated. CPR = cardiopulmonary resuscitation; NYHA = New York Heart Association. See Tables 1 and 3 for abbreviations not used in the text.

**Discussion**

This pilot study suggests that prehospital therapy with the GP IIb/IIIa inhibitor eptifibatide is feasible and safe in emergency situations in which patients are suspected of having an ACS or a STEMI. Treatment with eptifibatide prior to hospital admission led to an increase in the number of diagnostic angiographies performed during the subsequent hospital stay. GP IIb/IIIa therapy concomitant to acute PCI was continued in almost all patients who had been pretreated with eptifibatide in the ambulance, whereas in the control group a much smaller number of patients started receiving treatment with GP IIb/IIIa inhibitors. We gained the impression that patients having received eptifibatide beforehand showed fewer coronary artery occlusions with TIMI grade 0 or 1 blood flow during primary percutaneous transluminal coronary angioplasty than those in the control group. However, the survival rates as well as the rates of other cardiac and noncardiac complications were similar in both groups.

Previous studies investigating prehospital treatment focused on patients with STEMI that had been documented by a 12-lead ECG in the ambulance and early thrombolysis. The European Myocardial Infarction Study,10 in which 163 study centers in 15 different countries enrolled > 5,400 patients, was the largest study of this kind. The study revealed a 13% reduction (p = 0.08) in mortality among patients in the thrombolysis group. The indication to administer a thrombolytic agent was based on changes documented in a 12-lead ECG taken in the ambulance. Retrospectively, the diagnosis of a STEMI was subsequently confirmed in hospital in 87.6% of the patients included in the study, whereas 7.5% of the cases turned out to be a NSTEMI. In only 3% of patients was there either no indication for thrombolysis or thrombolysis was contraindicated. Unfortunately, any information regarding the percentage of patients with NSTEMI or STEMI actually being considered for prehospital thrombolysis in the ambulance was not given.

At present, there are no studies targeting the prehospital treatment of patients with ACS in addition to patients with definite or highly probable STEMI. There are also no data available yet referring to an experience with the prehospital application of GP IIb/IIIa inhibitors in the setting of emergency medical care in an ambulance.

Various factors already mentioned in the introduc-
tion, as well as locally specific factors, prompted us to initiate this pilot study of prehospital treatment with eptifibatide in an ambulance. The mere clinical suspicion of ACS or MI and the prehospital commencement of eptifibatide therapy, regardless of diagnostic confirmation by ECG or cardiac enzyme serology made in the ambulance, sufficed for inclusion in the study. The aim of this approach was to provide an opportunity to take a much broader range of patients with suspected ACS into consideration. Following admission to the hospital, the diagnosis ACS/STEMI was confirmed in 60% of the cases and refuted in 40%. In the latter group of patients, alternative diagnoses were made in which eptifibatide therapy was retrospectively not indicated or contraindicated in a few cases. There was no higher incidence of complications, particularly hemorrhages, seen in the eptifibatide group compared with patients in the control group. None of our patients experienced intracerebral bleeding as the most adverse hemorrhagic event. Similarly, in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy trial\(^1\) the risk of hemorrhagic stroke in 6,209 patients who had been treated with eptifibatide was \(< 0.1\%\), which was not different from that observed in the placebo group (4,739 patients).

Interestingly, pretreatment with eptifibatide led more frequently to treatment with GP IIb/IIIa inhibitors concomitant with the performance of PCI compared than in patients in the control group. It seems that hospital-based doctors are more inclined to continue with a preexisting treatment plan than to commence a new one. The majority of patients with troponin-positive ACS and STEMI underwent coronary angiography. The primary success rate of coronary interventions was almost identical in both study groups. Blinded analysis of coronary flow prior to intervention revealed lower rates of TIMI blood flow grades of 0 and 1 in target vessels in patients in the eptifibatide group. These findings should be interpreted very carefully, since neither the study design (ie, lack of randomization) nor the number of patients included in the study allows the drawing of significant conclusions. Our observations can at best serve as an indicator that GP IIb/IIIa inhibitor therapy initiated in the prehospital setting and subsequently continued may potentially improve the initial condition of the patients before they undergo primary PCI. This observation is in agreement with a previous brief communication\(^12\) demonstrating that the emergency department administration of eptifibatide before angioplasty resulted in a significantly higher incidence of partial or complete reperfusion in 30 patients with acute MI. Furthermore, this observation is in line with that of a meta-analysis\(^8\) showing that concurrent treatment with GP IIb/IIIa inhibitors can increase the benefit of PCI in patients with ACS. The relatively small number of patients in our pilot study allows no conclusions to be drawn regarding the clinical benefit of reducing infarct size or increasing survival rates.

In summary, our pilot study confirms the feasibility of prehospital treatment with GP IIb/IIIa inhibitors for patients with suspected ACS or STEMI. There was no evidence of increased risks caused by this type of treatment. However, the significance of any clinical benefit can be evaluated only by a large-scale, multicenter study.

**Limitations**

Alternate-day assignment is a deterministic method of allocation, but not an appropriate method of randomization, and it has relevant limitations. Since group assignments can be predicted in advance of assignment, participant allocation may be manipulated, causing selection bias. However, any randomization protocol is difficult to implement under emergency conditions. Thus, our approach was a practicable option for a best effort at randomization.

**References**


