Assessment of early administration of abciximab in acute ST-segment elevation myocardial infarction in the emergency room

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Summary
Objective > Abciximab, a platelet glycoprotein IIb/IIIa inhibitor, administered in conjunction with primary coronary stenting, improves the outcome of acute myocardial infarction, and the earlier it is administered, the greater the improvement. We sought to assess the feasibility of early administration of abciximab in the emergency room (ER) before primary coronary stenting and compare our results with those of a group of patients treated in the prehospital (ambulance) phase. Methods > Data and outcome of patients with acute ST-segment elevation myocardial infarction who received abciximab (0.25 mg.kg⁻¹ then 0.125 mg.kg⁻¹.h⁻¹) in the ER before primary coronary stenting were compared with those of patients who received abciximab in the prehospital phase. Results > Characteristics of the group treated in the ER did not differ significantly from those of patients treated before arrival at the hospital, except for prevalence of diabetes (22 versus 5%, p<0.05) and administration of analgesic to control chest pain (22 versus 65%, p<0.05). Nor did the median time between onset of pain and abciximab administration differ significantly different (120 versus 160 min,
n’étaient pas significativement différentes, à l’exception de l’incidence du diabète (22 versus 5%, \(p < 0.05\)) et de l’administration d’analgésiques pour la douleur thoracique (22 versus 65%, \(p < 0.05\)). Le temps médian entre le début de la douleur et l’administration de l’abciximab n’était pas significativement différent (120 versus 160 min, NS). En revanche, le délai médian entre l’administration d’abciximab et l’insertion du cathéter d’angioplastie était plus court dans le groupe SAU (35 versus 55 min, \(p < 0.05\)). Aucune différence significative n’était notée pour le grade TIMI avant et après la revascularisation coronaire et le pronostic.

**Conclusion** > Notre étude montre que l’administration précoce d’abciximab est faisable sans complication au SAU, et justifiée par les délais requis pour réaliser la revascularisation coronaire.

**What was known**

- **Abciximab**, a platelet glycoprotein IIb/IIIa inhibitor, when administered in conjunction with primary coronary stenting improves the outcome in acute myocardial infarction, and the earlier is the administration the better is the improvement.

**What this article adds**

- **We assessed the feasibility of the early administration of abciximab** in the emergency room before primary coronary stenting and compared our results with a group of patients treated in the prehospital phase.
- **Our study provides some evidence that the early administration of abciximab** in the emergency room is safe and feasible and justified by the delay required (median 35 min vs 55 min in the prehospital phase) for coronary revascularization.

**What this article adds**

- **Abciximab** administration and insertion of the cardiac catheter was significantly shorter in the ER group (35 versus 55 min, \(p<0.05\)). There were no significant differences between groups in TIMI flow grade before or after revascularization, specific revascularization performed, or outcome.

**Conclusion** > Our study provides some evidence that early administration of abciximab in the ER is safe, feasible, and justified by the delay required for coronary revascularization.

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**Methods**

Patients were eligible for this prospective study, which was conducted from June 2001 through November 2003, when they were diagnosed with acute ST-segment elevation myocardial infarction (AMI) and admission to a cardiac catheterization laboratory, transfer for primary PCI remains superior to local thrombolysis [2]. Platelet-mediated thrombosis is central to the pathophysiology of AMI. The combination of aspirin and ticlopidine enhances the benefit of coronary stenting by reducing acute stent thrombosis. Abciximab, a platelet glycoprotein IIb/IIIa inhibitor, administered in conjunction with primary coronary stenting for the treatment of AMI, improves PCI outcome [3, 4]. Most patients treated by abciximab, however, receive it very late, mainly during PCI. Meta-analysis shows that early administration of abciximab appeared to improve coronary patency and is associated with favorable trends for clinical outcome [5].

In our center, our prehospital team (ambulance, or Samu service) for several years has routinely administered abciximab early, in the ambulance, ever since its participation in the Admiral study [3]. Although transfer time to the catheterization laboratory is faster from the emergency room (ER) than from the ambulance, we decided to implement the same protocol in the ER. The primary objective of our study was to assess its feasibility and to compare the group of patients treated in the ER with the patients treated in the prehospital phase during the same period.

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Because the catheterization laboratory is located in a separate building of our hospital, patients were transferred from the ER to the cardiac catheterization laboratory in an ambulance and accompanied by an emergency physician as quickly as possible. Patients’ age, sex, and history were recorded, as well as heart rate and arterial blood pressure immediately after admission. A 12-lead electrocardiogram was performed immediately and faxed to the cardiologist for a decision about PCI. Killip status was recorded during physical examination [7]. Blood was taken for a troponin Ic assay (immunoenzymo-fluorometric assay on a Stratus autoanalyzer, Dade-Behring, La Défense, France) [8], but PCI was decided without awaiting its result. Troponin Ic values below 0.2 ng.mL⁻¹ were considered normal [9]. The time of the onset of chest pain, arrival in the emergency department, initial abciximab administration, arrival in the catheterization laboratory, and insertion of the cardiac catheter were all recorded.

Heparin (enoxaparin, [Lovenox®]) anticoagulation was given as required to prevent access site complications and deep vein thrombosis. The following adverse events were recorded: thrombopenia (<100 G.L⁻¹) and minor and major hemorrhagic complications. Major hemorrhage was defined as a hemorrhagic complication requiring transfusion or surgery or inducing shock or death.

**Statistical analysis**

Data are expressed as means ± SD or medians and their 95% confidence intervals (CI) for noncontinuous variables. Means were compared with Student’s t tests, medians with the Mann-Whitney test. We used the least-square method to assess correlations between variables and calculated the 95% CI of the slope. All P values were two-tailed and a P value less than 0.05 was considered significant. The NCSS 2001 statistical software program was used for all statistical analyses. The study was approved by the Ethics Committee of our hospital (Comité de Protection des Personnes se Prêtant à la Recherche Biomédicale Pitié-Salpêtrière, Paris). Since only routine care was performed, the committee waived the requirement for specific informed consent to study participation.

**Results**

During the study period, 23 patients received abciximab in the ER and 75 patients in the ambulance. During the same period, the ER saw 125 876 patients, 20 536 of whom were admitted to the hospital. Patients referred to the cardiac catheterization laboratory because of an elevated ST-segment myocardial infarction represented only 0.02% of ER patients and 0.11% of admitted patients.

All patients experienced chest pain. The only significant difference in the initial characteristics of patients in the two groups was prevalence of diabetes, which was higher in the ER group (table I). Killip status was 1 for all patients. Twenty patients in the ER group and none in the prehospital group had troponin Ic assays: results were within the normal range in 11 patients and elevated in 9. The groups did not differ significantly in the concomitant treatment received (table I), except for the treatment of coronary pain (figure 1).

Time elapsed between the onset of pain and abciximab administration did not differ significantly between the two groups (figure 2), although it varied more in the ER group, as the wider confidence interval shows. In the ER, median time from admission to abciximab administration was 52 min [95% CI: 40-80 min], and median time spent in the ER was 90 min [95% CI: 60-115 min]. Time from abciximab administration to the insertion of the cardiac catheter was significantly shorter in the ER group (figure 2).

![Figure 1](https://example.com/figure1.png)

**Figure 1**

Comparison of the proportion of patients receiving analgesic drugs (morphine) as part of the treatment of coronary pain by the prehospital team (n=49/75) and the Emergency Room (ER) staff (n=5/23).

**Table I**

<table>
<thead>
<tr>
<th>Patients’ characteristics</th>
<th>ER group (n=23)</th>
<th>Prehospital Group (n=75)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 ± 12</td>
<td>61 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>Man</td>
<td>17 (74%)</td>
<td>63 (84%)</td>
<td>NS</td>
</tr>
<tr>
<td>Woman</td>
<td>6 (26%)</td>
<td>12 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>Known coronary artery disease</td>
<td>6 (26%)</td>
<td>10 (13%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10 (43%)</td>
<td>24 (32%)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>8 (35%)</td>
<td>33 (44%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (22%)</td>
<td>4 (5%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Systolic arterial pressure (mmHg)</td>
<td>143 ± 23</td>
<td>143 ± 28</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>74 ± 17</td>
<td>74 ± 22</td>
<td>NS</td>
</tr>
<tr>
<td>Other medications administered before PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>21 (95%)</td>
<td>71 (95%)</td>
<td>NS</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>15 (68%)</td>
<td>40 (53%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: not significant; PCI: percutaneous coronary intervention

Data are mean ± SD or number (percentages).
Table II shows the results of the coronary angiography, the initial revascularization performed, and the TIMI flow grade in the occluded coronary artery before and after revascularization. There were no significant differences between groups. Coronary angiography was normal in 2 patients in the ER group. One patient in the ER group underwent a coronary artery bypass graft on the sixth day after percutaneous revascularization. One patient died in the ER group and 3 in the prehospital group (NS).

Table III summarizes the adverse effects reported with abciximab. They did not differ between the two groups. None of the patients with thrombopenia required platelet transfusion.

Discussion

Our study demonstrated the feasibility of abciximab treatment in the ER. Many studies have proven the efficacy of abciximab in AMI. US, European, and international guidelines [10, 11] now recommend its use, in association with standard antiplatelet therapy (aspirin), in patients with acute ST-segment elevation myocardial infarction, when PCI is to be performed. Because early treatment of AMI is very important in limiting complications, initiating anti-GPIIb/IIIa treatment as soon as AMI is diagnosed, before the patient arrives in the cardiology department, is likely to be useful.

The time elapsed between the onset of chest pain and abciximab administration was similar in both groups, although variability was greater in the ER group. It is similar to that observed in the Grape study (150 min) [13] and shorter than that in the Admiral study (178 to 238 min) [3]. The short delay between abciximab administration and initiation of PCI in the ER group is explained by the proximity of the two sites: once PCI is decided, the patient could be transferred quickly from one building to the other by a special ambulance. Delays were longer for the prehospital group because the patient first had to be driven to the PCI center. Nevertheless, the delay required inside the hospital to initiate PCI should not be underestimated. It includes the time required to transfer the patient, for the cardiologist to reach the

Table III

<table>
<thead>
<tr>
<th>Variables</th>
<th>ER group</th>
<th>Prehospital Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=23)</td>
<td>(n=75)</td>
</tr>
<tr>
<td>Thrombopenia</td>
<td>2 (9%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Minor hemorrhage</td>
<td>0</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Major hemorrhage</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>1 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>3 (13%)</td>
<td>3 (4%)</td>
</tr>
</tbody>
</table>

Data are number (percentages). p = not significant.
PCI laboratory, and for the patient to be prepared for PCI inside the coronary laboratory. Taken together, this duration is probably sufficient to justify early administration of abciximab in the ER. This delay may be shorter in hospitals where the cardiac catheterization laboratory is in the same building as the ER, or longer, when a transfer to another hospital is required.

Angiographic results before and after PCI were similar in both groups. The proportion of TIMI flow grade 3 (41 and 29%) in both groups was higher than in the studies without abciximab (8%) [14], and even higher than those previously observed in the abciximab groups of the Admiral and Grape studies (17 and 18%, respectively) [3, 13]. These effects are consistent with the hypothesis that abciximab has a thrombolytic effect [15] and support its early administration. Immediately after PCI, only two patients, both from the prehospital group still had a closed artery (TIMI flow grade 0), whereas all others had a TIMI flow grade of 2 or 3. In particular, 87% of the ER patients and 95% of the prehospital patients had an artery with a TIMI flow grade 3 after PCI. These results are similar to those of the Admiral study (95% of patients with a TIMI flow grade 3) [3] and consistent with findings that abciximab can improve the PCI results [16]. In a randomized study comparing early versus late administration of tirofiban, another platelet glycoprotein IIb/IIIa inhibitor, Lee et al. [17] showed that early administration safely improved coronary angiographic outcomes.

We must admit that all patients treated in the ER for acute myocardial infarction should ideally have been treated earlier, by our prehospital system. In France, patients with acute chest pain are expected to call the emergency phone number 15 and obtain rapid access to a prehospital team, so that arrival of a patient with acute myocardial infarction in the ER indicates a failure of the alert process. Public awareness of the need for and availability of rapid access to the prehospital team in cases of chest pain should probably be reinforced. Nonetheless, AMI will still be diagnosed in some cases in the ER, and thus emergency protocols, including abciximab administration and rapid referral to the cardiac laboratory are essential.

We noted two erroneous diagnoses (3%) of acute myocardial infarction in the ER group: their coronary angiography was normal. Their chest pain has since been attributed to myocarditis and pericarditis. Nevertheless, abciximab had no observable adverse effects in these patients.

Control of chest pain is an important part of the management of patients with acute myocardial infarction [18]. This message has obviously been understood and applied by the prehospital emergency physicians whereas it remains ignored by most of the in-hospital emergency physicians (figure 2). This observation is consistent with the rather poor management of acute pain observed in many emergency departments [9]. The abciximab protocols should therefore clearly include pain control, mainly morphine [20] with an intravenous titration protocol [21].

We have some remarks about the weaknesses of our study. First, our study power is low, in view of the relatively few patients included. This is because most patients with segment ST elevation AMI acute myocardial infarction in France are taken by the prehospital teams directly to the cardiology department: few arrive directly to the ER. Second, since this study was not randomized, we cannot reach a direct conclusion about the efficacy of abciximab in the ER. Nevertheless, previous randomized studies have already proven its efficacy [3-5, 17].

In conclusion, in light of the efficacy of abciximab in this indication [3-5] and the apparent beneficial effects of its early administration [6, 17], our study provides some evidence that its early administration in the ER is safe, feasible and justified by the delay that precedes PCI.

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