Intracoronary Compared With Intravenous Bolus Abciximab Application in Patients With ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

The Randomized Leipzig Immediate Percutaneous Coronary Intervention Abciximab IV Versus IC in ST-Elevation Myocardial Infarction Trial

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Background—Abciximab reduces major adverse cardiac events in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention (PCI). Intracoronary abciximab bolus application results in high local drug concentrations and may be more effective than a standard intravenous bolus.

Methods and Results—Patients undergoing primary PCI were randomized to either intracoronary (n=77) or intravenous (n=77) bolus abciximab administration with subsequent 12-hour intravenous infusion. The primary end point was infarct size and extent of microvascular obstruction as assessed by delayed enhancement magnetic resonance. Secondary end points were ST-segment resolution at 90 minutes, Thrombolysis in Myocardial Infarction flow and perfusion grades after PCI, and the occurrence of major adverse cardiac events within 30 days. The median infarct size was 15.1% (interquartile range, 6.1% to 25.2%) in the intracoronary versus 23.4% (interquartile range, 13.6% to 33.2%) in the intravenous group (P=0.01). Similarly, the extent of microvascular obstruction was significantly smaller in intracoronary compared with intravenous abciximab patients (P=0.01). Myocardial perfusion measured as early ST-segment resolution was significantly improved in intracoronary patients with an absolute ST-segment resolution of 77.8% (interquartile range, 66.7% to 100.0%) versus 70.0% (interquartile range, 45.2% to 83.5%; P=0.006). The Thrombolysis in Myocardial Infarction flow after PCI was not different between treatment groups (P=0.51), but there was a trend toward an improved perfusion grade (P=0.09). There also was a trend toward a lower major adverse cardiac event rate after intracoronary versus intravenous abciximab application (5.2% versus 15.6%; P=0.06; relative risk, 0.33; 95% CI, 0.09 to 1.05).

Conclusions—Intracoronary bolus administration of abciximab in primary PCI is superior to standard intravenous treatment with respect to infarct size, extent of microvascular obstruction, and perfusion. (Circulation. 2008;118:49-57.)

Key Words: angioplasty ■ infarction ■ magnetic resonance imaging ■ platelets ■ reperfusion

In patients with acute ST-elevation myocardial infarction, primary percutaneous coronary intervention (PCI) is the preferred reperfusion regimen if performed by experienced operators in a timely manner. Nevertheless, myocardial damage is not immediately terminated after successful epicardial reperfusion by primary PCI. Current strategies are directed at improving myocardial tissue perfusion, which is impaired in ~50% of patients and has prognostic impact. Adjunctive abciximab administration is an established therapy to improve coronary microcirculation and reduces major cardiac adverse events. Intravenous abciximab administration has been studied in randomized clinical trials. Intracoronary abciximab bolus administration with very high local platelet inhibitor concentrations may be favorable in dissolution of thrombi and microemboli with subsequent improved myocardial microcircula-
tion and reduced no reflow and infarct size.10-11 Currently, clinical experience in the efficacy of intracoronary abciximab administration is limited.12-16

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Therefore, the aim of this randomized trial was to assess the effects of intracoronary versus intravenous abciximab bolus administration on the occurrence of no reflow and infarct size assessed by contrast-enhancement magnetic resonance imaging.

**Methods**

**Patients**

From February through November 2006, we randomly assigned in an open-label fashion 154 consecutive patients with ST-elevation myocardial infarction undergoing primary PCI to either intracoronary or intravenous bolus abciximab (0.25 mg/kg body weight) administration with subsequent 12-hour intravenous infusion at a dose of 0.125 μg/kg per minute (maximum, 10 μg/min). Balanced randomization was performed by drawing sealed unlabeled envelopes placed in no order in an urn. Inclusion criteria were the presence of symptoms <12 hours and ST-segment elevation of at least 0.1 mV in ≥2 extremity leads or at least 0.2 mV in ≥2 precordial leads. Exclusion criteria were prior fibrinolysis; known allergy to heparin, aspirin, or abciximab; active severe bleeding; pregnancy; history of major surgery <4 weeks; and cardiogenic shock with mechanical ventilation. Furthermore, patients with contraindications to magnetic resonance imaging at study entry such as implanted pacemakers, defibrillators, or metallic intracranial implants were excluded. The study was approved by the local ethics committee, and all patients gave written informed consent.

**Study Protocol**

Per protocol, the abciximab bolus administration should be performed before PCI. In the intracoronary group, bolus administration was recommended after infarct-related artery recanalization by the PCI wire before balloon dilatation to allow high abciximab concentration in the target region. The bolus was administered directly within 1 minute through the PCI guiding catheter. Filtering was performed before the abciximab solution was pulled into the syringe. In cases with extreme short door-to-balloon times, abciximab bolus administration was allowed to be performed after PCI because of the predominant importance of timely optimized reperfusion. All patients received 500 mg aspirin and heparin (60 U/kg body weight) intravenously before PCI. Stenting of the culprit vessel, as defined previously.17,18 Visual assessments were performed offline in the angiographic core laboratory by 2 blinded observers (G.F. and L.E.).

**Angiographic Analysis**

Coronary angiography of the target lesion was performed before and after PCI with the same projections. Angiographic projections used were those that allowed optimal evaluation of the Thrombolysis in Myocardial Infarction (TIMI) flow and TIMI perfusion grades of the infarct-related artery or the myocardium supplied by it.17,18 Angiographic analysis included initial and final flow and perfusion of the culprit vessel, as defined previously.17,18 Visual assessments were performed offline in the angiographic core laboratory by 2 blinded observers (G.F. and L.E.).

**ST-Segment Resolution**

For ECG interpretation, blinded observers (J.F. and L.E) measured the sum of ST-segment elevation 20 ms after the end of the QRS complex in the ECG before and that obtained early after PCI after transfer to the intensive care unit. ST-segment resolution was calculated as the sum of ST elevation before minus the sum of ST elevation after PCI divided by the sum of ST elevation before PCI. ST-segment resolution was expressed as a percentage.19

**Infarct Size Measured by Enzyme Release**

The infarct size was measured indirectly by the area under the curve of the creatine kinase release derived from measurements every 6 hours over 2 days.

**Magnetic Resonance Imaging**

Myocardial infarct size and microvascular obstruction were determined by magnetic resonance imaging at day 1 to 4 after the index event. Imaging was performed on a 1.5-T scanner (Philips Intera CV, Best, the Netherlands). Left ventricular function was assessed by a standard steady-state free precession technique.20 For acute infarct determination, 3 short-axis slices using a T2-weighted turbo spin-echo sequence were obtained.21,22 Early and delayed enhancement images covering the whole ventricle were acquired ~1 and 15 minutes after intravenous administration of 0.15 mmol/kg body weight gadobutrol (Gadovist, Schering, Germany) with an inversion recovery gradient echo sequence.23 The inversion time was adapted individually to null normal myocardium. All measurements were performed by fully blinded operators (K.S. and H.T.) at the magnetic resonance core laboratory, which has excellent intraobserver and interobserver variabilities and excellent reproducibility for infarct size measurement.24 Left ventricular ejection fraction and end-diastolic and end-systolic volumes were calculated from the short-axis views. Total left ventricular myocardial mass and infarct size, expressed as a percentage of left ventricular mass, were assessed manually as described previously.25 Extent of microvascular obstruction in early and delayed images was determined similarly by manual drawing of the obstructed area within the infarction of the short-axis slices and expressed as a percentage of the left ventricular mass.

**End Points**

The primary end point was final infarct size and microvascular obstruction extent assessed by contrast-enhanced magnetic resonance imaging. Secondary end points were early ST-segment resolution of no reflow and infarct size measured by magnetic resonance imaging. The angiographic TIMI flow and perfusion grades after PCI,17,18 and infarct size measured by the area under the curve of creatine kinase release. The clinical secondary end point was a composite of major adverse cardiovascular events defined as a composite of death, reinfarction, urgent target vessel revascularization, and occurrence of new congestive heart failure within 30 days after randomization. Posthospital follow-up included 1 outpatient visit at 30 days. The diagnosis of reinfarction was based on clinical symptoms, new ST-segment changes, and an increase in the creatine kinase and MB levels above the reference limits in patients with normalized values after the index event or if there was an increase of at least 50% from the last nonnormalized measurement. New heart failure was defined as any congestive heart failure (rales, dyspnea New York Heart Association class III to IV) occurring ≥24 hours after the index event. Outcomes were adjudicated by clinical events committee members (G.S., E.G., and H.T.) who were unaware of the patient’s assigned treatment.

**Statistical Analysis**

The number of patients included in this study was based on the primary end point of infarct size and extent of microvascular obstruction. From previous trials and a pilot trial, we projected a final infarct size of 20±10% (5±4% microvascular obstruction) after
intravenous abciximab administration.\textsuperscript{24–27} With a power of 80\% and
a 2-sided $\alpha$ value of 0.05, we estimated that 68 patients would be
required in each group to detect an absolute difference of 5\% in
infarct size (2\% microvascular obstruction). A total of 154 patients
were included to allow for the possibility of missing magnetic
resonance imaging studies. Predefined subgroup analysis was per-
formed for anterior/nonanterior infarction, postprocedural angio-
graphic flow and perfusion grades 3 versus 3, and different times
from symptom onset to reperfusion (4 versus 4 to 12 hours). Each
categorical variable is expressed as a number and percentage of
patients. Continuous parameters were estimated as median with
interquartile range. Differences between treatment groups were
assessed by Fisher’s exact or the $\chi^2$ test for categorical variables and
by the Student $t$ test for continuous data with normal distribution.
Otherwise, the nonparametric Wilcoxon rank-sum test was used. For
the combined secondary clinical end point, the Kaplan-Meier method
was applied, and differences were assessed by the log-rank test. All
statistical tests were performed with SPSS software version 14.0
(SPSS Inc, Chicago, Ill). A 2-tailed value of $P<0.05$ was considered
statistically significant.

The authors had full access to and take responsibility for the
integrity of the data. All authors have read and agree to the
manuscript as written.

**Results**

Of the 154 patients enrolled, 77 were randomly assigned to
intracoronary and 77 to intravenous abciximab administration
(Figure 1). This was an all-comers study, and no eligible
patients were excluded during the study period. All patients
received the assigned treatment. The baseline characteristics
and medication were similar between groups (Table 1).
Abciximab bolus administration was performed in all pa-
tients. Before PCI, it was accomplished in 83\% in the
intracoronary and 77\% in the intravenous group ($P=0.42$).
Discontinuation of glycoprotein IIb/IIIa inhibitor administra-
tion was necessary in 4 (n=2 groin bleeding, n=1 hema-
mesis, n=1 pericardial effusion) intracoronary and 5 (n=3
groin bleeding, n=1 pericardial effusion, n=1 diffuse bleed-
ing caused by thrombocytopenia) intravenous group patients
($P=0.93$). There were no adverse events during intracoronary
abciximab bolus administration. Reperfusion times were
similar with a median time from symptom onset to PCI of 244
minutes (interquartile range, 163 to 433 minutes) and 218
minutes (interquartile range, 159 to 323 minutes; $P=0.47$),
respectively. Thirty-seven (49\%) and 46 (60\%) patients were
treated within the first 4 hours after symptom onset ($P=0.20$).
The door-to-balloon time was 31 minutes (interquartile range,
22 to 40 minutes) versus 29 minutes (interquartile range, 21
to 40 minutes; $P=0.77$).

**Infarct Size and Microvascular Obstruction**

Results of magnetic resonance imaging were available in 67
(87\%) of the intracoronary and in 71 (92\%) of the intravenous
abciximab group patients (Figure 1). The median time be-
tween randomization and magnetic resonance imaging was 2
days (interquartile range, 2 to 3 days) for both groups
($P=0.94$). The primary end point of infarct size was signif-
ically smaller after intracoronary compared with intravenous
abciximab bolus administration. Similarly, the extent of
microvascular obstruction was smaller in the intracoronary
than the intravenous group at early and late imaging (Table 2). However, left ventricular ejection fraction and end-diastolic and end-systolic volume indexes were similar between both groups at this early stage after the index event (Table 2).

The primary end points of infarct size and microvascular obstruction also were analyzed in several predefined subgroups. Patients with anterior infarction had greater benefit from intracoronary versus intravenous abciximab bolus administration with respect to infarct size (16.7% [interquartile range, 9.5% to 28.4%] versus 28.0% [interquartile range, 16.1% to 41.0%]; \( P = 0.04 \)) and early (2.1% [interquartile range, 0.0% to 5.1%] versus 4.3% [interquartile range, 0.35% to 13.2%]; \( P = 0.06 \)) and late microvascular obstruction. There were no differences in infarct size and microvascular obstruction for patients undergoing reperfusion \(<4\) hours after symptom onset. For patients undergoing reperfusion \(>4\) hours after symptom onset, intracoronary abciximab bolus administration resulted in smaller infarct size (13.0% [interquartile range, 6.9% to 24.3%] versus 22.2% [interquartile range, 14.1% to 31.3%]; \( P = 0.002 \)) and less early (1.1% [interquartile range, 0.0% to 3.6%] versus 3.5% [interquartile range, 0.1% to 5.8%]; \( P = 0.04 \)) and late (0.1% [interquartile range, 0.0% to 1.4%] versus 0.8% [interquartile range, 0.0% to 2.2%]; \( P = 0.03 \)) microvascular obstruction. There also was a greater benefit for intracoronary abciximab infusion in patients with impaired TIMI flow and perfusion grades after PCI. These results are given in Figure 2a and 2b.

**Table 1. Main Patient Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intracoronary Abciximab (n=77)</th>
<th>Intravenous Abciximab (n=77)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64 (54–70)</td>
<td>66 (54–73)</td>
<td>0.33</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>63 (82)</td>
<td>59 (77)</td>
<td>0.73</td>
</tr>
<tr>
<td>Current smoking</td>
<td>38 (49)</td>
<td>39 (51)</td>
<td>0.98</td>
</tr>
<tr>
<td>Hypertension</td>
<td>54 (70)</td>
<td>57 (74)</td>
<td>0.72</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>27 (35)</td>
<td>31 (40)</td>
<td>0.62</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24 (31)</td>
<td>22 (29)</td>
<td>0.86</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>8 (10)</td>
<td>7 (9)</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior coronary artery bypass grafting, n (%)</td>
<td>0</td>
<td>2 (3)</td>
<td>0.97</td>
</tr>
<tr>
<td>Anterior myocardial infarction, n (%)</td>
<td>44 (57)</td>
<td>40 (52)</td>
<td>0.63</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>127 (106–145)</td>
<td>125 (110–137)</td>
<td>0.60</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>76 (65–83)</td>
<td>70 (62–81)</td>
<td>0.14</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>80 (72–90)</td>
<td>77 (67–90)</td>
<td>0.20</td>
</tr>
<tr>
<td>Diseased vessels, n (%)</td>
<td></td>
<td></td>
<td>0.89</td>
</tr>
<tr>
<td>1</td>
<td>40 (52)</td>
<td>37 (48)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>24 (31)</td>
<td>26 (34)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>13 (17)</td>
<td>14 (18)</td>
<td></td>
</tr>
<tr>
<td>Killip class on admission, n (%)</td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>1</td>
<td>53 (69)</td>
<td>51 (66)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>17 (22)</td>
<td>21 (27)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5 (7)</td>
<td>5 (7)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2 (3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Concomitant medications, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \beta )-Blockers</td>
<td>76 (99)</td>
<td>76 (99)</td>
<td>1.00</td>
</tr>
<tr>
<td>ACE inhibitors/AT-1 antagonist</td>
<td>76 (99)</td>
<td>77 (100)</td>
<td>0.97</td>
</tr>
<tr>
<td>Aspirin</td>
<td>77 (100)</td>
<td>77 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>77 (100)</td>
<td>77 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Statins</td>
<td>76 (99)</td>
<td>77 (100)</td>
<td>0.97</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>10 (13)</td>
<td>10 (13)</td>
<td>1.00</td>
</tr>
<tr>
<td>Completion of abciximab infusion</td>
<td>73 (95)</td>
<td>72 (94)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting enzyme; AT-1, angiotensin-1. Continuous data are presented as median (interquartile range).
Correlation between enzymatic and magnetic resonance infarct size was good for intracoronary and intravenous abciximab administration ($r = 0.86$ and $0.75$, $P < 0.001$ for both; Figure 3).

### ST-Segment Resolution

In 2 intracoronary abciximab patients, the ST-segment resolution was not interpretable because these patients required pacing as a result of atrioventricular block grade 3. The median time between the first and second ECGs was 148 minutes (interquartile range, 112 to 171 minutes) in the intracoronary and 128 minutes (interquartile range, 102 to 164 minutes) in the intravenous group ($P = 0.40$). ST-segment resolution as a continuous variable was significantly better in the intracoronary abciximab group (77.8% [interquartile range, 66.7% to 100.0%] versus 70.0% [interquartile range, 45.2% to 83.5%]; $P = 0.006$).

### Angiographic Analysis

The TIMI flow and TIMI perfusion grades before PCI were similar (Table 3). After PCI, the majority of patients had a TIMI grade 3 flow (84.4% versus 85.7%, respectively). In the intracoronary abciximab group, there was a trend toward improved TIMI perfusion grade after PCI ($P = 0.09$; Table 3).

### Clinical Outcome

At the 30-day follow-up, there were 2 cardiac deaths (2.6%) in the intracoronary and 3 (3.9%) in the intravenous abciximab group. Nonfatal reinfarctions occurred in 0 subjects after intracoronary and in 2 (2.6%) after intravenous abciximab application. The need for target vessel revascularization was identical (0 versus 2 [2.6%]). New congestive heart failure occurred in 2 (2.6%) and 5 (6.5%) patients, respectively. Thus, the composite major adverse cardiac event rate at the 30-day follow-up was 5.2% after intracoronary and 15.6% after intravenous abciximab administration (relative risk, 0.33; 95% CI, 0.09 to 1.05; $P = 0.06$; Figure 4).

### Discussion

This first adequately powered randomized clinical trial of intracoronary versus intravenous abciximab administration in patients undergoing primary PCI for ST-elevation myocardial infarction showed a reduction in microvascular obstruction extent and infarct size as assessed by magnetic resonance imaging, which is a state-of-the-art imaging technique. Furthermore, myocardial tissue perfusion assessed by ST-segment resolution was significantly better after intracoronary abciximab bolus administration. This resulted in a trend toward better clinical outcome with respect to a combined clinical end point. However, in the acute setting after the index event, there was no improvement in left ventricular function and volumes.

### Table 2. Results of Magnetic Resonance Imaging

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intracoronary Abciximab (n=67)</th>
<th>Intravenous Abciximab (n=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct size, % of LV</td>
<td>15.1 (6.1–25.2)</td>
<td>23.4 (13.6–33.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>MO early, % of LV</td>
<td>1.1 (0.0–3.7)</td>
<td>3.4 (0.1–7.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>MO late, % of LV</td>
<td>0.1 (0.0–1.6)</td>
<td>1.1 (0.0–2.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>48.0 (38.5–52.7)</td>
<td>46.1 (36.4–50.4)</td>
<td>0.71</td>
</tr>
<tr>
<td>LV end-diastolic volume index, mL/m²</td>
<td>79.5 (70.4–90.6)</td>
<td>73.6 (65.4–89.2)</td>
<td>0.65</td>
</tr>
<tr>
<td>LV end-systolic volume index, mL/m²</td>
<td>42.9 (33.4–53.8)</td>
<td>42.5 (34.0–53.4)</td>
<td>0.97</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>68.4 (58.3–77.1)</td>
<td>67.7 (59.2–78.4)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

LV indicates left ventricle; MO, microvascular obstruction. Data are presented as median (interquartile range). Volumes and mass are normalized to body surface area.

Figure 2. A, Differences in infarct size and early and late microvascular obstruction in percentage of the left ventricle (%LV) for TIMI flow <3 and 3 for intracoronary (▫) and intravenous (▫) abciximab bolus administration. There were 10 patients (14.9% and 14.1%) in each group with TIMI flow <3 after PCI. B, Differences in infarct size and early and late microvascular obstruction in percentage of the left ventricle for TIMI perfusion grade <3 and 3 for intracoronary (▫) and intravenous (▫) abciximab bolus administration. There were 18 patients in the intracoronary (26.9%) and 23 in the intravenous (32.4%) abciximab group with TIMI perfusion grade <3 after PCI. The boxes plot the median, 25th and 75th (interquartile range) percentiles, and smallest and largest observation as vertical boxes with error bars. Black points indicate outliers.
These beneficial effects of intracoronary abciximab administration might be explained by the high local doses, which may facilitate the diffusion of the antibody to platelets inside the flow-limiting thrombus, thus resulting in improved dissolution of thrombi and microemboli at the ruptured plaque and further downstream in the microcirculation. Therefore, by protocol, the bolus administration was recommended after thrombus penetration by the PCI guidewire to achieve very high local concentration. This could not be accomplished in all patients as a result of the very short door-to-balloon times when preparation of the abciximab bolus took longer than PCI. The higher local concentration effects are supported by the larger effects on infarct size and microvascular obstruction in patients with postinterventional impaired flow and perfusion. Depending on the relation of inflow and outflow and the size of the ischemic area, the local abciximab concentration can vary substantially. However, even in situations with restitution of normal flow and perfusion in the infarct-related artery, intracoronary abciximab bolus administration will result in very high local concentrations, which might be much higher than the usual intravenous application mode that reduces platelet aggregation to <20% within 10 minutes.28 Another potential mechanism of high local concentrations might be related to the antiinflammatory properties of abciximab.7 These clinical considerations are supported by experimental data showing a dose-dependent platelet disaggregation. Concentrations that produced complete platelet disaggregation also induced partial displacement of platelet-bound fibrinogen, which might play a role in the clinical setting.29

Previous trials assessing the effect of intracoronary abciximab administration were limited to case reports, retrospective registries, and small randomized trials.12–16 In one of these trials, angiographic reperfusion was improved in the intracoronary abciximab group as assessed by the corrected TIMI frame count. Furthermore, there was a trend toward lower infarct size as assessed by cardiac enzymes.15 In a small randomized clinical trial of 45 patients, there was a significantly higher degree of myocardial salvage with subsequent
lower infarct size as assessed by serial scintigraphy. In another randomized trial of 137 patients, lower troponin I levels after PCI were observed. There was no improved clinical outcome, which might be due to the low-risk patient subgroup; <50% had ST-segment elevation. The present results with regard to infarct size and microvascular obstruction might explain the improved clinical outcome after intracoronary abciximab administration that was evident in the present trial and 2 previous retrospective registries of 403 and 173 patients.14,16

An important factor is timing of glycoprotein IIb/IIIa inhibitor administration. Clinical trials have shown that earlier administration results in higher preinterventional TIMI flow with subsequent improved perfusion after PCI.30,31 However, in a pooled analysis and a recently published trial, there was no effect on mortality or clinical end points.32,33 Because the door-to-balloon-times were extremely short in a highly experienced tertiary care center in the present trial, earlier abciximab administration requires treatment in the prehospital setting, which poses substantial logistical obstacles. Early complete ST-segment resolution >70% was observed in 50% to 59% in the early-administration–treated patients, which is comparable to the intravenous group in our trial but lower than in the intracoronary group.10,31 Similarly, the angiographic perfusion grade after PCI was similar between the intravenous group and previously published results, whereas the intracoronary group had nonstatistically significant higher perfusion grades.31

Infarct size as an end point in reperfusion trials has been advocated because of its potential prognostic value.34 We used a sensitive and reliable method, which, compared with scintigraphic studies, has the advantage of higher spatial resolution with the ability to detect even small subendocardial infarcts and allows a sample size reduction because of its accuracy.24,35,36 In addition, magnetic resonance imaging allows assessment of microvascular obstruction, which has prognostic impact.37,38 Currently, there is no consensus on the best imaging technique for assessment of microvascular obstruction.37,38 As a consequence, we measured microvascular obstruction at 2 different time points, which revealed a previously described reduction in microvascular obstruction over time.38 From a theoretical point of view, magnetic resonance can be used for measurement of myocardial salvage but has not yet been applied in humans.22 Therefore, we used only 3 short-axis slices of T2-weighted images for the delineation of chronic and acute myocardial infarction in patients with previous infarction.21,22

Mechanisms underlying impaired myocardial perfusion after restoration of epicardial blood flow are likely to be multifactorial such as oxygen free radicals, cellular and interstitial edema, endothelial dysfunction, vasoconstriction, and thromboembolism.2,39 The secondary angiographic and electrocardiographic end points are well established for the assessment of perfusion at the epicardial and microvascular levels. However, the TIMI flow and perfusion grades might
be too insensitive to detect differences in the very early setting after abciximab bolus administration.\textsuperscript{17,18} In contrast, the sensitive ECG assessment at a later measurement reflected improved tissue perfusion.\textsuperscript{19}

A limitation is that this trial had sufficient statistical power only to assess final infarct size and extent of microvascular obstruction. Confirmation of the results with respect to clarification of the long-term effects on ventricular size and function and, more important, on clinical outcome requires a larger trial. Although all angiographic, ECG, and magnetic resonance imaging measurements were blinded, patients and interventionists were aware of the group assignment. Thus, a potential investigator bias cannot be ruled out entirely. Some patients had to be excluded from magnetic resonance infarct size assessment. Because the number of patients in both groups was identical and the baseline characteristics of patients undergoing and those not undergoing magnetic resonance imaging were similar, a potential selection bias is limited.

Conclusions

Intracoronary bolus administration of abciximab is superior to standard intravenous treatment with respect to reduction in infarct size, extent of microvascular obstruction, and improvement of perfusion in primary PCI. An adequately powered trial for clarification of this approach on the long-term benefit on ventricular function, ventricular volumes, and improvement of perfusion in primary PCI is needed. This adequately powered trial for clarification of this approach on the long-term benefit on ventricular function, ventricular volumes, and improvement of perfusion in primary PCI is warranted.

Disclosures

None.

References

Abciximab reduces major adverse cardiac events in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Intracoronary abciximab bolus application results in high local drug concentrations and consequently might be more effective than a standard intravenous bolus. In the present randomized, controlled trial, intracoronary abciximab bolus application with subsequent 12-hour continuous intravenous infusion showed reduced no reflow and infarct size as assessed by contrast-enhanced magnetic resonance imaging. Furthermore, myocardial perfusion measured by early ST-segment resolution was significantly better in patients treated by intracoronary abciximab application, and there was a trend toward improved angiographic perfusion. On the other hand, there was no increased risk from this direct application. If the infarct size and no-reflow reduction and the improvement in perfusion can be translated into an improved clinical outcome, a larger trial powered to detect differences in outcome will be warranted.
Intracoronary Compared With Intravenous Bolus Abciximab Application in Patients With ST-Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention: The Randomized Leipzig Immediate Percutaneous Coronary Intervention Abciximab IV Versus IC in ST-Elevation Myocardial Infarction Trial
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