Intracoronary Abciximab and Aspiration Thrombectomy in Patients With Large Anterior Myocardial Infarction
The INFUSE-AMI Randomized Trial

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PRIMARY PERCUTANEOUS CORONARY intervention (PCI) is widely accepted as the most effective reperfusion modality for ST-segment elevation myocardial infarction (STEMI). However, myocardial recovery after primary PCI is often suboptimal despite restoration of coronary blood flow, in part due to thrombus embolization resulting in impaired microvascular perfusion.1-4 Two strategies proposed to reduce distal embolization after primary PCI are bolus intracoronary abciximab5-8 and manual aspiration thrombectomy.9-13

The mechanism through which reduced embolization and improved myocardial recovery after primary PCI is mediated is not well understood. A possible explanation is that bolus abciximab reduces thrombus embolization by reducing surface area and/mass of the embolized clot, thereby improving microvascular perfusion.14-17 It is also possible that aspirated thrombus reduces myocardial edema, which might improve myocardial perfusion.18-22 Manual aspiration thrombectomy reduces thrombus embolization by removing the thrombus from the coronary circulation.19,23-26

Intracoronary abciximab and manual aspiration thrombectomy may also improve myocardial perfusion by reducing late thrombus formation.27,28 In addition, abciximab inhibits platelets and provides additional antithrombotic protection, thereby inhibiting new thrombus formation.29-32 Manual aspiration thrombectomy removes thrombus from the coronary circulation, which may reduce microvascular irritation and/or improve coronary flow through guidewire traversal.33-36

In STEMI, the cardiac magnetic resonance imaging (cMRI) technique provides the ability to assess infarct size, ventricular function, and microvascular perfusion in a uniform, standardized manner, while also allowing for quantitative myocardial perfusion.37-40 Our study aimed to determine whether bolus intracoronary abciximab, manual aspiration thrombectomy, or both reduce infarct size in high-risk patients with STEMI. We compared 30-day infarct size in patients randomized to bolus intracoronary abciximab vs no abciximab and to manual aspiration thrombectomy vs no thrombectomy.

Methods

Study Population

The primary study population included patients enrolled in the INFUSE-AMI trial.41 Enrollment criteria included patients aged 18 years or older presenting with an ST-segment elevation myocardial infarction (STEMI) within 4 hours of symptom onset, with ST-segment elevation in ≥2 contiguous leads, and with proximal or mid left anterior descending artery occlusion. The study population consisted of 452 patients enrolled at 37 sites in 6 countries between November 28, 2009, and December 2, 2011. Patients were randomized to bolus intracoronary abciximab vs no abciximab and to manual aspiration thrombectomy vs no thrombectomy. The randomized groups were based on local site preferences and investigator experience. The study was approved by the institutional review boards of all participating centers, and informed consent was obtained from all patients or from their legal representatives.

Study Design

Patients enrolled in the INFUSE-AMI trial were randomized in an open-label, 2×2 factorial design to bolus intracoronary abciximab administered at the site of the infarct lesion via a local drug delivery catheter vs no abciximab and to manual aspiration thrombectomy performed with a 6-F aspiration catheter vs no thrombectomy. Intracoronary abciximab was delivered as a 0.25-mg/kg bolus at the site of the infarct lesion. Manual aspiration thrombectomy was performed with a 6-F aspiration catheter, which was placed in the distal coronary segment or side branch, and activated at the site of thrombus aspiration. Manual aspiration was performed until thrombus was not aspirated into the suction port of the aspiration catheter. The device was removed when there was no further yield of thrombus. The local site investigator determined the need for additional passes and the number of passes required to remove thrombus from the coronary circulation.

Study End Points

The primary end point was infarct size (percentage of total left ventricular mass) at 30 days, assessed with cMRI in the abciximab vs no abciximab groups (pooled across the aspiration randomization). A major secondary end point was 30-day infarct size in the aspiration vs no aspiration groups (pooled across the abciximab randomization).

Results

Of the 452 randomized patients, 253 were randomized to abciximab and 227 to no abciximab, 237 were randomized to aspiration thrombectomy and 227 to no thrombectomy. Patients randomized to intracoronary abciximab compared with no abciximab had a significant reduction in 30-day infarct size (median, 15.1%; interquartile range [IQR], 6.8%-22.7%; n=181, vs 17.9% [IQR, 10.3%-25.4%]; n=172; P=.03). Patients randomized to intracoronary abciximab also had a significant reduction in absolute infarct mass (median, 18.7 g [IQR, 7.4-31.3 g]; n=184, vs 24.0 g [IQR, 12.1-34.2 g]; n=175; P=.03) but not abnormal wall motion score (median, 7.0 [IQR, 2.0-10.0]; n=188, vs 8.0 [IQR, 3.0-10.0]; n=184; P=.08). Patients randomized to aspiration thrombectomy vs no aspiration had no significant difference in infarct size at 30 days (median, 17.0% [IQR, 9.0%-22.8%]; n=174, vs 17.9% [IQR, 7.1%-25.5%]; n=179; P=.51), absolute infarct mass (median, 20.3 g [IQR, 9.7-31.7 g]; n=178, vs 21.0 g [IQR, 9.1-34.1 g]; n=181; P=.36), or abnormal wall motion score (median, 7.5 [IQR, 2.0-10.0]; n=186, vs 7.5 [IQR, 2.0-10.0]; n=186; P=.89).

Conclusion

In patients with large anterior STEMI presenting early after symptom onset and undergoing primary PCI with bivalirudin anticoagulation, infarct size at 30 days was significantly reduced by bolus intracoronary abciximab delivered locally at the infarct lesion site but not by manual aspiration thrombectomy.
cardial perfusion may improve clinical outcomes is enhanced myocardial salvage. However, conflicting results have been reported as to whether intracoronary abciximab and manual aspiration thrombectomy reduce infarct size or improve clinical outcomes, in part because of differences in patient selection, devices, and study methodology. Moreover, many patients enrolled in these trials had a small amount of myocardium at risk (eg, non-anterior MI); presented up to 12 hours after infarct onset, well beyond the time window for effective myocardial salvage; or both. Also, no such prior trial has been performed in patients undergoing primary PCI with bivalirudin as the procedural anticoagulant, which has been shown to reduce major bleeding and improve survival compared with heparin plus a glycoprotein IIb/IIIa inhibitor.

We therefore performed a multicenter, prospective trial in which patients presenting early with anterior STEMI and proximal or mid left anterior descending (LAD) artery occlusion undergoing primary PCI with bivalirudin were randomized in a factorial design to bolus intracoronary abciximab vs no abciximab and to manual aspiration thrombectomy vs no aspiration.

**METHODS**

The design of the INFUSE-AMI trial has been previously described. INFUSE-AMI was an open-label, factorial, randomized, multicenter, single-blind evaluation of bolus intracoronary abciximab and manual aspiration thrombectomy in patients undergoing primary PCI for anterior STEMI. The study was approved by the institutional review board at each participating center, and all eligible patients signed informed, written consent.

Patients 18 years and older with symptoms consistent with STEMI longer than 30 minutes’ duration and 1 mm or greater of ST-segment elevation in 2 or more contiguous leads in V₁-V₄, or new left bundle-branch block, with anticipated symptom-onset-to-device time of 5 hours or less (ie, symptom-to-presentation time, ≤3.5-4 hours) were eligible for enrollment. Principal clinical exclusion criteria included contraindications to study medications or contrast; prior MI, bypass graft surgery, or LAD stenting; planned surgery necessitating antiplatelet agent interruption; contraindication to cardiac magnetic resonance imaging (cMRI); known creatinine clearance less than 30 mL/min/1.73 m², dialysis, platelet count less than 100,000 or greater than 700,000 cells/mm³, or hemoglobin level less than 10 g/dL; recent major bleeding, bleeding diathesis, or current warfarin use; history of intracranial disease; ischemic stroke or transient ischemic attack within 6 months or any permanent neurologic defect; prerandomization cardiogenic shock or cardiopulmonary resuscitation; prior fibrinolysis or IIb/IIIa inhibitor for the present admission; and any comorbid conditions likely to interfere with protocol compliance or associated with less than 1-year survival.

Patients were administered aspirin, 324 mg orally or 250 to 500 mg intravenously, and clopidogrel, 600 mg, or prasugrel, 60 mg, after which emergent coronary arteriography and left ventriculography were performed. Patients undergoing PCI received procedural anticoagulation with bivalirudin (intravenous bolus 0.75 mg/kg plus infusion of 1.75 mg/kg per hour, discontinued at procedure end) without routine glycoprotein IIb/IIIa inhibition. Angiographic eligibility required the infarct lesion to be located in the proximal or mid LAD with visually assessed Thrombolysis in Myocardial Infarction (TIMI) 0-2 flow, and absence of excessive tortuosity, diffuse disease, heavy calcification, or significant left main disease.

Eligible patients were randomized equally to 1 of 4 groups: (1) thrombus aspiration followed by intracoronary bolus abciximab, (2) thrombus aspiration without abciximab, (3) intracoronary bolus abciximab without aspiration, or (4) no abciximab and no aspiration. Telephone randomization in block sizes of 8 within strata was performed using a computerized interactive voice response system balancing for time from symptoms to angiography less than 3 hours vs 3 or more hours and by proximal vs mid LAD occlusion.

Manual thrombus aspiration was performed with a 6 F Export Catheter (Medtronic), the same device used in the TAPAS (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study). The protocol specified actively aspirating whenever crossing the lesion or withdrawing the catheter, making several passes until no further thrombus or debris was retrieved. To ensure high intrathrombus drug concentrations, a 0.25-mg/kg bolus of abciximab was administered locally at the site of the infarct lesion via the ClearWay RX Local Therapeutic Infusion Catheter, a microporous “weeping” PTFE balloon mounted on a 2.7F rapid exchange catheter (Atrium Medical). An abciximab infusion after PCI was allowed only for refractory intraprocedural thrombotic complications. Percutaneous coronary intervention was performed using standard techniques, with bare metal or drug-eluting stent implantation at operator discretion. (See video of procedural coronary angiograms of a patient treated with thrombus aspiration followed by intracoronary bolus abciximab at http://www.jama.com.)

After PCI, all patients were treated with aspirin indefinitely and with clopidogrel or prasugrel for at least 1 year. Cardiac MRI was scheduled in all patients at 30 days. Clinical follow-up was scheduled at 30 days and at 1 year. The enrolling research coordinator and local principal investigator performing the index procedure were aware of the study assignments. The patient and all subsequent study personnel, including follow-up nurses, core laboratory technicians, the clinical event adjudication committee, the executive com-
mittee, and the sponsor, were blinded to the randomized treatment.

End Points and Definitions
Baseline patient data for demographic characteristics and medication use, presenting signs and symptoms, laboratory results, 12-lead electrocardiography, and coronary angiography were collected. The primary efficacy end point was infarct size (percentage of total left ventricular mass) at 30 days in patients assigned to intracoronary abciximab vs no abciximab (pooled across the thrombectomy randomization). The major secondary end point was 30-day infarct size in patients assigned to aspiration thrombectomy vs no thrombectomy (pooled across the abciximab randomization). Additional efficacy end points included measures of angiographic reperfusion (TIMI flow, myocardial blush grade [MBG]), ST-segment resolution (STR) at 60 minutes, and 30-day and 1-year clinical outcomes. Cardiac MRI (eMethods and eFigure, available at http://www.jama.com), angiographic, and STR end points were evaluated at independent core laboratories,2,3 blinded to randomization and outcomes.

Major adverse cardiac events (MACE) were defined as death, reinfarction, new-onset severe heart failure, or rehospitalization for heart failure. Major adverse cardiac and cerebrovascular events (MACCE) were defined as death, reinfarction, stroke, or clinically driven target vessel revascularization (TVR). Bleeding was assessed using the HORIZONS-AMI, TIMI, and GUSTO Bleeding scales. Detailed definitions of the clinical end points have been previously published.18 An independent clinical events committee blinded to randomization adjudicated all major end point events using original source documents.

Statistical Methods
The study was powered for infarct size determination at 30 days. A relative reduction in infarct size of 25% with either randomized therapy was considered clinically relevant. Evaluating 408 participants randomized to intracoronary abciximab vs no abciximab provided 80% power to demonstrate a relative 25% reduction in infarct size from 24% to 18% (with SD 21%). To account for loss to follow-up and suboptimal cMRI, enrollment was planned for 452 patients. To preserve a formal hypothesis testing of the major secondary end point of infarct size in patients randomized to aspiration vs no aspiration was performed only if the primary end point of infarct size with intracoronary abciximab vs no abciximab was significantly reduced.

All analyses were performed by intention to treat. Missing data were not replaced. However, multiple imputation for missing baseline data and outcomes was performed as a sensitivity analysis for the principal infarct size end points, using the prespecified baseline variables of left ventricular ejection fraction, proximal vs mid left LAD lesion, presence of angiographic collateral vessels, time from symptom onset to first device, sex, and age. Categorical outcomes were compared by χ² or Fisher exact test. Continuous variables are presented as median with interquartile range (IQR) and compared by Wilcoxon rank sum test. Analysis of variance models were performed to exclude significant interactions between the 2 levels of randomization. As infarct size is nonnormally distributed, nonparametric testing was used for the principal analysis of the primary and major secondary end points. Infarct size is also reported as mean with standard deviation and compared by t test. Kaplan-Meier time-to-event estimates for clinical outcomes were compared with log-rank test. All statistical tests were 2-sided. A P value less than .05 was considered significant for all analyses. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc).

RESULTS
Between November 28, 2009, and December 2, 2011, 6,318 patients with STEMI were screened at 37 sites in 6 countries (United States, Germany, Poland, Austria, the Netherlands, and the United Kingdom), 452 (7.2%) of whom were randomized (Figure). The most common reasons for exclusion were nonanterior MI and symptom-to-treatment time greater than 5 hours. The baseline characteristics of the 4 randomized groups were well matched (Table 1).

Procedural data for the patients assigned to intracoronary abciximab vs no abciximab (pooled across the thrombectomy randomization) and those assigned to aspiration thrombectomy vs no thrombectomy (pooled across the abciximab randomization) appear in Table 2. A bolus of abciximab was administered to 223 of 229 abciximab-randomized patients (97.4%); in all but 1 patient, abciximab was infused locally to the infarct lesion site through the drug delivery study catheter. Manual thrombus aspiration was performed in 225 of 229 aspiration-randomized patients (98.3%). The prespecified aspiration catheter was used in all but 3 cases, and visible thrombus was retrieved from 78.9% of patients.

Discharge medications included aspirin in 99.1% of patients, clopidogrel in 66.4%, prasugrel in 31.8%, statins in 97.7%, β-blockers in 96.6%, and an angiotensin-converting enzyme inhibitors or receptor blockers in 94.1%, with no significant differences between groups.

Myocardial Perfusion and ST-Segment Resolution
Post-PCI TIMI 3 flow, an MBG of 2 or 3, and complete STR at 60 minutes were achieved in 91.4%, 81.4%, and 53.7% of patients, respectively. No significant differences in these measures were present between patients randomized to intracoronary abciximab vs no abciximab or to aspiration thrombectomy vs no thrombectomy (Table 2 and eTable 1).

Infarct Size and Clinical Outcomes
Cardiac MRI was performed in 382 of 439 patients (87.1%) alive at 30 days, from which wall motion and infarct size were analyzable by the core labora-
tory in 372 and 353 patients, respectively (Figure). Patients randomized to intracoronary abciximab compared with no abciximab had a significant decrease in the primary end point of infarct size measured as a percentage of total myocardial mass (median, 15.1% [IQR, 6.8%-22.7%] vs 17.9% [IQR, 10.3%-25.4%]; \( P = .03 \); mean [SD], 15.2% [9.9%] vs 17.5% [10.2%]; difference, −2.3% [95% CI, −4.4% to −0.2%]; \( P = .03 \)) and absolute infarct mass, but not in abnormal wall motion score (Table 3 and eTable 2).

Patients randomized to aspiration thrombectomy vs no aspiration had no significant difference in infarct size (median, 17.0% [IQR, 9.0%-22.8%] vs median, 17.3% [IQR, 7.1%-25.5%]; \( P = .51 \); mean [SD], 15.9% [9.7%] vs 17.5% [10.6%]; difference, 0.7% [95% CI, −2.9% to 1.4%]; \( P = .49 \)), absolute infarct mass, or abnormal wall motion score (Table 3 and eTable 2). After multiple imputation to adjust for missing baseline and outcomes data, assignment to intracoronary abciximab vs no abciximab was associated with a nominal reduction in infarct size at 30 days (median, 15.4% [IQR, 7.0%-22.7%] vs 17.6% [IQR, 10.2%-24.7%]; mean difference, −2.0% [95% CI, −4.0% to −0.0%]; \( P = .0498 \)), whereas no significant difference in infarct size was present in patients randomized to manual aspiration vs no aspiration (median, 16.6% [IQR, 8.8%-22.7%] vs 17.4% [IQR, 7.3%-25.2%]; mean difference, −1.1% [95% CI, −3.1% to 0.9%]; \( P = .27 \)).

Cardiac MRI at 30 days was performed in only 2 of 31 patients (6.5%)

More than 1 reason for study exclusion were present in some patients who were not eligible for randomization. Cardiac magnetic resonance imaging (cMRI) at 30 days was not performed in 70 enrolled patients for the following reasons: patient refusal or withdrawn consent for cMRI (n = 27); patient inability to complete the cMRI (most commonly for claustrophobia) (n = 15); death before the 30-day cMRI (n = 13); too ill (n = 4); patient forgot (n = 4); contrast contraindication (n = 2); other (n = 5). In addition, despite being performed, the cMRI study was not evaluable for the primary end point of infarct size in 29 patients because of technical issues in image acquisition, including incorrect image sequencing, inadequate inversion recovery time, excessive breathing artifact, and missing slices. CAGB denotes coronary artery bypass graft; GPI, glycoprotein IIb/IIIa inhibitor; IC, intracoronary; LAD, left anterior descending coronary artery; PCI, percutaneous coronary intervention; and TIMI, Thrombolysis in Myocardial Infarction.
in whom MACE occurred, in 1 patient treated with intracoronary abxiximab with no aspiration, and in 1 patient treated with no abxiximab and no aspiration.

No interaction was present between the 2 randomization groups for the 30-day infarct size end point (P=.46), although in a post hoc analysis, median infarct size was lowest in the intracoronary abxiximab plus aspiration group compared with the other 3 groups combined (median, 14.7% [IQR, 7.1%-20.6%] vs 17.6% [IQR, 8.1%-25.1%]; P=.03).

No significant differences in any of the major safety or efficacy end points were present between the randomized groups at 30 days (Table 4 and eTable 3).

**COMMENT**

The principal findings from this multicenter, prospective, randomized trial in patients presenting early in the course of a large evolving anterior STEMI undergoing primary PCI with bivalirudin anticoagulation are as follows: (1) bolus intracoronary abxiximab delivered to the infarct lesion site significantly but modestly reduced the primary end point of infarct size at 30 days; (2) in contrast, manual aspiration thrombectomy did not significantly reduce infarct size; and (3) indices of myocardial reperfusion, STR, and 30-day clinical event rates were not significantly different between the randomized groups.

The present study was designed to maximize the likelihood that a reduction in infarct size could be demonstrated with intracoronary abxiximab, aspiration thrombectomy, or both, if indeed such a reduction truly exists. Two of the strongest baseline determinates of infarct size are anterior MI location and abnormal TIMI flow.19 We therefore limited enrollment to patients with proximal or mid LAD occlusion (and without prior MI) and operator-assessed baseline TIMI 0-2 flow. We also restricted enrollment to patients who could be treated early, in whom the time window for effective myocardial salvage had not closed.14 Indeed, the median time from symptom onset to hospital arrival was only 99 minutes, and the median door-to-device time was 45 minutes. The study population thus represents a highly selected cohort of patients with large anterior MI (those with the greatest clinical need), in whom infarct size reduction should be feasible given early presentation and rapid treatment.

We assessed infarct size by cMRI, which strongly correlates with subsequent mortality.4,20,21 To reduce sample size, prior studies using cMRI have typically measured infarct size early after reperfusion (2-7 days), a period during which substantial myocardial edema is present that may be mischaracterized as nonviable myocardium.22,23 We therefore powered the present trial for assessment of the primary infarct size end point at 30 days (when much of the myocardial edema has resolved), a time

### Table 1. Baseline Characteristics of the Randomized Groups

<table>
<thead>
<tr>
<th>Patients, No./Total No. (%)</th>
<th>Aspiration + IC Abciximab (n = 118)</th>
<th>No Aspiration + IC Abciximab (n = 111)</th>
<th>Aspiration + No Abciximab (n = 111)</th>
<th>No Aspiration + No Abciximab (n = 112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>60.0 (52.0-66.0)</td>
<td>56.0 (49.0-68.0)</td>
<td>62.0 (53.0-73.0)</td>
<td>62.5 (52.5-71.0)</td>
</tr>
<tr>
<td>Male sex</td>
<td>84/118 (71.2)</td>
<td>84/111 (75.7)</td>
<td>85/111 (76.6)</td>
<td>81/112 (72.3)</td>
</tr>
<tr>
<td>Body mass index, median (IQR)</td>
<td>26.6 (23.9-29.7)</td>
<td>26.3 (23.8-29.4)</td>
<td>26.8 (24.3-30.5)</td>
<td>26.8 (24.0-28.7)</td>
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<tr>
<td>Killip class</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>99/118 (83.9)</td>
<td>96/111 (86.5)</td>
<td>82/110 (74.5)</td>
<td>90/112 (80.4)</td>
</tr>
<tr>
<td>II</td>
<td>8/118 (6.8)</td>
<td>6/111 (5.4)</td>
<td>13/110 (11.8)</td>
<td>13/112 (11.6)</td>
</tr>
<tr>
<td>III</td>
<td>2/118 (1.7)</td>
<td>2/111 (1.8)</td>
<td>0/110 (0)</td>
<td>2/111 (1.8)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>37/118 (31.4)</td>
<td>30/111 (27.0)</td>
<td>39/111 (35.1)</td>
<td>36/112 (32.1)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>20/117 (17.1)</td>
<td>19/111 (17.1)</td>
<td>18/111 (16.2)</td>
<td>14/112 (12.5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15/118 (12.7)</td>
<td>9/111 (8.1)</td>
<td>19/110 (17.3)</td>
<td>8/112 (7.1)</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>0/118</td>
<td>3/110 (2.7)</td>
<td>1/110 (0.9)</td>
<td>0/112</td>
</tr>
<tr>
<td>Prior percutaneous coronary intervention</td>
<td>2/118 (1.7)</td>
<td>2/110 (1.8)</td>
<td>3/111 (2.7)</td>
<td>3/112 (2.7)</td>
</tr>
<tr>
<td>Cigarette smoking, current</td>
<td>52/117 (44.4)</td>
<td>52/109 (48.6)</td>
<td>46/109 (42.2)</td>
<td>55/112 (49.1)</td>
</tr>
<tr>
<td>Symptom to hospital arrival, median (IQR), min</td>
<td>92.5 (65.0-152.0)</td>
<td>100.5 (75.0-158.0)</td>
<td>107.0 (86.5-152.5)</td>
<td>98.0 (67.0-136.0)</td>
</tr>
<tr>
<td>Hospital arrival to first device, median (IQR), min</td>
<td>43.0 (30.0-64.0)</td>
<td>48.0 (36.0-69.0)</td>
<td>42.0 (30.0-61.0)</td>
<td>46.5 (34.0-70.3)</td>
</tr>
<tr>
<td>Symptom onset to first device, median (IQR), min</td>
<td>141 (120-221)</td>
<td>166 (126-233)</td>
<td>151 (117-205)</td>
<td>160 (126-217)</td>
</tr>
<tr>
<td>Infarct artery lesion location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal left anterior descending</td>
<td>74/118 (62.7)</td>
<td>76/111 (68.5)</td>
<td>68/111 (61.3)</td>
<td>74/112 (66.1)</td>
</tr>
<tr>
<td>Mid left anterior descending</td>
<td>49/118 (41.5)</td>
<td>44/111 (39.6)</td>
<td>47/111 (42.3)</td>
<td>48/112 (42.9)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, median (IQR), %</td>
<td>40.0 (35.0-49.0)</td>
<td>40.0 (35.0-48.0)</td>
<td>40.0 (38.0-50.0)</td>
<td>40.0 (31.0-50.0)</td>
</tr>
</tbody>
</table>

Abbreviations: IC, intracoronary; IQR, interquartile range.
A Calculated as weight in kilograms divided by height in meters squared.
B Balloon angioplasty, local drug delivery, or aspiration.
C Some patients had both proximal and mid left anterior descending lesions.
D From contrast left ventriculography during the index procedure.

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more specific for identification of truly infarcted myocardium. Myocardial reperfusion was assessed by several complementary parameters, including post-PCI TIMI flow, MBG, and STR. In addition, bivalirudin was used as the procedural anticoagulant to minimize bleeding and improve survival. Under these optimal conditions, 30-day infarct size was significantly reduced by intracoronary abciximab but not by manual aspiration thrombectomy, representing the primary and major secondary end points of the trial, respectively.

### Table 2. Procedural Outcomes and Reperfusion Indices for the Pooled Randomized Groups

<table>
<thead>
<tr>
<th>Patients, No./Total No. (%)</th>
<th>Intracoronary Abciximab&lt;sup&gt;a&lt;/sup&gt; (n = 229)</th>
<th>No Intracoronary Abciximab&lt;sup&gt;a&lt;/sup&gt; (n = 223)</th>
<th>P Value</th>
<th>Aspiration Thrombectomy&lt;sup&gt;b&lt;/sup&gt; (n = 229)</th>
<th>No Aspiration Thrombectomy&lt;sup&gt;b&lt;/sup&gt; (n = 223)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unfractionated heparin administered before cardiac catheterization</td>
<td>142/229 (62.0)</td>
<td>145/223 (65.0)</td>
<td>.51</td>
<td>145/229 (63.3)</td>
<td>142/223 (63.7)</td>
<td>.94</td>
</tr>
<tr>
<td>Bivalirudin administered</td>
<td>229/229 (100.0)</td>
<td>222/223 (99.6)</td>
<td>&lt;.001</td>
<td>116/229 (50.7)</td>
<td>112/223 (50.2)</td>
<td>.93</td>
</tr>
<tr>
<td>Abciximab administered</td>
<td>223/229 (97.4)</td>
<td>5/223 (2.2)</td>
<td>&lt;.001</td>
<td>116/229 (50.7)</td>
<td>112/223 (50.2)</td>
<td>.93</td>
</tr>
<tr>
<td>Aspiration performed</td>
<td>119/229 (52.0)</td>
<td>115/223 (51.6)</td>
<td>.93</td>
<td>225/229 (98.3)</td>
<td>9/223 (4.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of lesions treated, mean (SD)</td>
<td>1.1 (0.4)</td>
<td>1.2 (0.4)</td>
<td>.28</td>
<td>1.2 (0.4)</td>
<td>1.2 (0.4)</td>
<td>.64</td>
</tr>
<tr>
<td>Drug-eluting stents implanted</td>
<td>171/229 (74.7)</td>
<td>157/223 (70.4)</td>
<td>.31</td>
<td>170/229 (74.2)</td>
<td>158/223 (70.9)</td>
<td>.42</td>
</tr>
<tr>
<td>Total stent length, median (IQR), mm</td>
<td>24.0 (18.0-34.0)</td>
<td>23.0 (17.0-32.5)</td>
<td>.13</td>
<td>23.5 (18.0-32.0)</td>
<td>24.0 (18.0-35.0)</td>
<td>.30</td>
</tr>
<tr>
<td>Maximum stent diameter, median (IQR), mm</td>
<td>3.0 (3.0-3.5)</td>
<td>3.0 (3.0-3.5)</td>
<td>.75</td>
<td>3.0 (3.0-3.5)</td>
<td>3.0 (3.0-3.5)</td>
<td>.20</td>
</tr>
<tr>
<td>TIMI flow before PCI&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0/1</td>
<td>166/229 (72.5)</td>
<td>158/223 (70.9)</td>
<td>.70</td>
<td>168/229 (73.4)</td>
<td>156/223 (70.0)</td>
</tr>
<tr>
<td>2/3</td>
<td>63/229 (27.5)</td>
<td>65/223 (29.1)</td>
<td>.70</td>
<td>61/229 (26.6)</td>
<td>67/223 (30.0)</td>
<td>.42</td>
</tr>
<tr>
<td>TIMI flow after PCI&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0/1</td>
<td>7/229 (3.1)</td>
<td>4/223 (1.7)</td>
<td>.18</td>
<td>4/229 (1.7)</td>
<td>5/223 (2.2)</td>
</tr>
<tr>
<td>2</td>
<td>13/229 (5.7)</td>
<td>17/223 (7.6)</td>
<td>.41</td>
<td>13/229 (5.7)</td>
<td>17/223 (7.6)</td>
<td>.41</td>
</tr>
<tr>
<td>3</td>
<td>209/229 (91.3)</td>
<td>204/223 (91.5)</td>
<td>.94</td>
<td>212/229 (92.6)</td>
<td>201/223 (90.1)</td>
<td>.36</td>
</tr>
<tr>
<td>Corrected TIMI frame count after PCI, median (IQR)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>20 (16-26)</td>
<td>20 (16-26)</td>
<td>.62</td>
<td>20 (16-26)</td>
<td>20 (16-26)</td>
<td>.40</td>
</tr>
<tr>
<td>MBG 0/1 after PCI&lt;sup&gt;c&lt;/sup&gt;</td>
<td>44/228 (19.3)</td>
<td>40/223 (17.9)</td>
<td>.71</td>
<td>38/229 (16.6)</td>
<td>46/222 (20.7)</td>
<td>.26</td>
</tr>
<tr>
<td>MBG 2/3 after PCI&lt;sup&gt;c&lt;/sup&gt;</td>
<td>184/228 (80.7)</td>
<td>183/223 (82.1)</td>
<td>.71</td>
<td>191/229 (83.4)</td>
<td>176/222 (79.3)</td>
<td>.26</td>
</tr>
</tbody>
</table>

### Table 3. Thirty-Day Cardiac Magnetic Resonance Imaging Results for the Pooled Randomized Groups

<table>
<thead>
<tr>
<th>Intracoronary Abciximab&lt;sup&gt;a&lt;/sup&gt; (n = 188)</th>
<th>No Intracoronary Abciximab&lt;sup&gt;a&lt;/sup&gt; (n = 184)</th>
<th>P Value</th>
<th>Aspiration Thrombectomy&lt;sup&gt;b&lt;/sup&gt; (n = 186)</th>
<th>No Aspiration Thrombectomy&lt;sup&gt;b&lt;/sup&gt; (n = 186)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct size, median [IQR], % of total LV mass&lt;sup&gt;c&lt;/sup&gt;</td>
<td>15.1 [6.8-22.7]</td>
<td>17.9 [10.3-25.4]</td>
<td>.03</td>
<td>17.0 [9.0-22.8]</td>
<td>17.3 [7.1-25.5]</td>
</tr>
<tr>
<td>Total LV myocardial mass, median [IQR], g</td>
<td>128.6 [106.6-152.4]</td>
<td>130.4 [109.9-155.9]</td>
<td>.55</td>
<td>128.3 [108.9-149.8]</td>
<td>132.0 [107.6-156.1]</td>
</tr>
<tr>
<td>Infarct mass, median [IQR], g</td>
<td>18.7 [7.4-31.3]</td>
<td>24.0 [12.1-34.2]</td>
<td>.03</td>
<td>20.3 [9.7-31.7]</td>
<td>21.0 [9.1-34.1]</td>
</tr>
<tr>
<td>Total abnormal wall motion score, median [IQR]</td>
<td>7.0 [2.0-10.0]</td>
<td>8.0 [3.0-10.0]</td>
<td>.08</td>
<td>7.5 [2.0-10.0]</td>
<td>7.5 [2.0-10.0]</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, median [IQR], %</td>
<td>50.2 [44.2-57.9]</td>
<td>48.9 [42.3-56.7]</td>
<td>.22</td>
<td>49.6 [43.3-56.8]</td>
<td>49.5 [41.8-57.6]</td>
</tr>
</tbody>
</table>

Abbreviations: MBG, myocardial blush grade; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.
<sup>a</sup>Pooled, either with or without aspiration thrombectomy.
<sup>b</sup>Pooled, either with or without intracoronary abciximab.
<sup>c</sup>Core laboratory assessed.
<sup>d</sup>In patients with baseline ST-segment elevation in 2 or more contiguous leads.
These results need to be placed in the context of previous studies. Two earlier randomized trials demonstrated infarct size reductions with intracoronary compared with intravenous abciximab (despite enrollment of patients with nonanterior MI presenting up to 12 hours after symptoms), and a meta-analysis of 6 randomized trials (1246 patients) reported enhanced survival with intracoronary abciximab (despite enrollment of patients with nonanterior MI presenting up to 12 hours after symptoms), and a meta-analysis of 6 randomized trials (1246 patients) reported enhanced survival with intracoronary abciximab. However, the recently completed AIDA-STEMI trial, which with 2065 randomized patients was powered for clinical outcomes, found nearly identical rates of MACE (and biomarker-assessed infarct size) with bolus intracoronary and intravenous abciximab.

However, in addition to enrolling only anterior STEMI patients presenting early, our trial differs from these earlier studies in several important ways. First, all prior studies of intracoronary vs intravenous abciximab included a 12-hour post-PCI abciximab infusion in both groups. Procedural anticoagulation with bivalirudin without routine glycoprotein IIb/IIIa inhibition in the control group of INFUSE-AMI thus isolated the effects of bolus-only abciximab. Second, in all prior trials (including AIDA-STEMI), intracoronary abciximab was infused proximally through the guide catheter, limiting its penetration into occlusive thrombus and allowing preferential drug flow to lower resistance pathways (such as the left circumflex artery) and blowback into the aorta. In contrast, the local drug delivery catheter used in the present study directly achieves high intraclot concentrations of abciximab at the site of LAD occlusion and prolongs drug residence time, which may enhance platelet disaggregation and thrombus resolution. In the present study, an abciximab bolus delivered directly to the infarct lesion site (without a 12-hour infusion) reduced infarct size at 30 days (the primary end point of the study) in patients with anterior STEMI reperfused early.

Regarding aspiration thrombectomy, in TAPAS, 1071 patients with anterior and nonanterior STEMI who presented within 12 hours of symptom onset at a single center were randomized to manual aspiration (using the same catheter as studied in the present study). The results of this trial are presented in Table 4.
Moreover, studies have not shown greater thrombus retrieval or improved myocardial perfusion with larger bore devices,29 and use of a larger aspiration catheter in a prior randomized trial was associated with increased infarct size.12

Fifth, infarct size assessment by cMRI at 30 days was available in only 353 of 452 patients (78.1%), with the most common reasons for missing data being patient death prior to 30 days, inability to tolerate the procedure, patient refusal or withdrawal, and study site technical issues with image acquisition. Of note, however, the 78.1% acquisition rate in the present study at 30 days is similar to 81.6% cMRI infarct size acquisition rate at 3 to 5 days reported from the recently published CRISP AMI trial.30

In addition, although infarct size at 30 days was reduced with intracoronary abciximab, early markers of microcirculatory reperfusion (MBG and STR) were not improved. This discordance may reflect different ascertainment times given infarct evolution over 30 days (especially as edema is substantially reduced during this time) and variable accuracy of different biomarkers. The comparable 30-day clinical event rates between groups is consistent with the early MBG and STR results.2,3 Moreover, the magnitude of the absolute reduction in infarct size with intracoronary abciximab, while statistically significant, was modest (mean reduction, 2.3%; 95% CI, 0.2% to 4.4%, of total left ventricular mass, less than the 6% which was considered clinically relevant during planning of the study). As a result, the increase in left ventricular ejection fraction noted in abciximab-treated patients compared with those not receiving abciximab did not reach statistical significance. Larger trials are required to determine whether the degree of infarct size reduction at 30 days achieved with intracoronary abciximab in the present study translates into improved late clinical outcomes without increasing bleeding.

In conclusion, among patients with large anterior STEMI presenting early after infarct onset and undergoing primary PCI with bivalirudin anticoagulation, infarct size was reduced by bolus intracoronary abciximab delivered to the site of the infarct lesion, but not by manual aspiration thrombectomy.

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Study supervision: Stone, Ochala, Carlton, Wolff, Chowdhary, El-Omar, Neunteufl, Metzger, Karwoski, Dizon, Gibson.

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Abbott Vascular, Boston Scientific, Evotec, AstraZeneca, Eli Lilly and Company, Bristol-Myers Squibb-Sanofi partnership, Otsuka, The Medicines Company, Ortho-McNeil, Atrium, Gilead, InspireMD, TherOx, Volcano, InfraReDx, Genentech, GlaxoSmithKline, Miracor, MPF Group, and Lutonix; has received honoraria from Edwards and Vascular Solutions; and holding stock or options from CoreValve, Savacor, Biostar I and II funds, MedFocus I, II, and Accelerator funds, Calliber, Flowcardia, Medigus, Guided Delivery Systems, Ovalum, Anstatis, Micardia, Access Closure, Embrella and VNT. Dr Witzenbichler reports having served on advisory boards for Boston Scientific and Biotronik and receiving lecture honoraria from Boston Scientific, Biotronik, Medtronic, and The Medicines Company. Mr Carlton and Mr Kanowski being employed by Atrium Medical. Dr Wolff reports receiving honoraria and royalties from GE Healthcare and is the founder of Soft and NeoCoil. Dr Brener reports having served as a consultant for Medtronic and receiving lecture honoraria for Eli Lilly. Dr Neunteufl reports having served on editorial boards for Acta Cardiologica, Bacterg Trials, Biotronik, Boston Scientific, Eli Lilly-Daichi Sankyo, and St Jude and having received lecture fees from Abbott Vascular, AstraZeneca, Atrium, Boston Scientific, Ed- wards Lifesciences-Daichi Sankyo and sanofi-aventis. Dr Metzger reports serving as a consultant for Abbott Vascular, Medtronic, Lutonix, IDEV, Cook Medical, and Cordis Endovascular and has received lecture fees, travel reimbursements, and honoraria from Abbott, Cardiovascular, an IDEV, Pathway, and St Jude Medical. Dr Mehran reports serving as a consultant for Abbott Vascular, AstraZeneca, Ortho McNeil, and Regado Biosciences and receiving grants from BMS/sanofi-aventis. Dr McNeill reports having served as a consultant for Biogen IDEC, Bristol Meyer Squibb, Daichi Sankyo, CSL Behring, Cytori Therapeutics, Eli Lilly, GlaxoSmithKline, Genentech, Japan Tobacco, and Johnson & Johnson McNeil, Merck, Portola Pharmaceuticals, Regado Biosciences, sanofi-aventis, St Jude, The Medicines Company, Medicure, Archheim, and Boeringer Ingelheim; having received lecture fees from Daichi Sankyo, Eli Lilly, and The Medicines Company; receiving royalties from UpToDate in CV Medicine; and having received payments for development of educational presentations from Daichi Sankyo and Eli Lilly. The other authors report no disclosures.

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Role of the Sponsor: Atrium Medical was involved in the design and conduct of the study and site selec- tion and had the right to a nonbinding review of the manuscript. The sponsor provided standard funding to the clinical sites for patient enrollment and fees to the Cardiovascular Research Foundation for core laboratory analyses, clinical events adjudication, and data management and biostatistical analysis, and interpretation of the data or in the prepa- ration or approval of the manuscript. Medtronic had the right to a nonbinding review of the manuscript but had no role in the design and conduct of the study; in the collection, management, analysis, and interpreta- tion of the data; or in the preparation or approval of the manuscript. The Medicines Company had no role in the study other than supplying bivalirudin for the study participants and did not review the manuscript prior to its submission. No agreements exist regar- ding data confidentiality.

Individual Statistical Analysis: Helen Parise, from the Cardiovascular Research Foundation and Columbi- a University College of Physicians and Surgeons, was responsible for all data analyses. Ms Parise controlled the database and applied the necessary filters and performed all data analyses reported in the article.

REFERENCES


INTRACORONARY ABCIXIMAB AND ASPIRATION THROMBECTOMY IN MI


