Intracoronary Versus Intravenous Administration of Abciximab in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention With Thrombus Aspiration

The Comparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) Trial

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Background—Administration of the glycoprotein IIb/IIIa inhibitor abciximab is an effective adjunctive treatment strategy during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Although small-scale studies have suggested beneficial effects of intracoronary over intravenous administration of abciximab, this has not been investigated in a medium-scale randomized clinical trial.

Methods and Results—A total of 534 ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with thrombus aspiration within 12 hours of symptom onset were randomized to either an intracoronary or an intravenous bolus of abciximab (0.25 mg/kg). Patients were pretreated with aspirin, heparin, and clopidogrel. The primary end point was the incidence of restored myocardial reperfusion, defined as complete ST-segment resolution. Secondary end points included myocardial reperfusion as assessed by myocardial blush grade, enzymatic infarct size, and major adverse cardiac events at 30 days. The incidence of complete ST-segment resolution was similar in the intracoronary and intravenous groups (64% versus 62%; \( P = 0.562 \)). However, the incidence of myocardial blush grade 2/3 was higher in the intracoronary group than in the intravenous group (76% versus 67%; \( P = 0.022 \)). Furthermore, enzymatic infarct size was smaller in the intracoronary than in the intravenous group (\( P = 0.008 \)). The incidence of major adverse cardiac events was similar in both groups (5.5% versus 6.1%; \( P = 0.786 \)).

Conclusions—In ST-segment elevation myocardial infarction patients undergoing primary percutaneous coronary intervention with thrombus aspiration, intracoronary administration of abciximab compared with intravenous administration does not improve myocardial reperfusion as assessed by ST-segment resolution. However, intracoronary administration is associated with improved myocardial reperfusion as assessed by myocardial blush grade and a smaller enzymatic infarct size.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00927615.

Key Words: acute myocardial infarction ■ angioplasty ■ glycoproteins IIb-IIIa ■ myocardial reperfusion

ST-segment elevation myocardial infarction (STEMI) is a clinical condition caused by rupture or erosion of an atherosclerotic plaque and subsequent platelet aggregation and thrombosis, resulting in acute occlusion of a coronary artery.\(^1\)\(^,\)\(^2\) Prompt reperfusion therapy with primary percutaneous coronary intervention (PCI) has become the treatment strategy of choice.\(^3\)\(^,\)\(^4\) Recently, the implementation of adjunctive mechanical and pharmacological therapies dur-
ing primary PCI, including manual thrombus aspiration and glycoprotein (GP) IIb/IIIa inhibitors, has improved myocardial reperfusion and clinical outcome in STEMI patients.\textsuperscript{5-9} In large randomized trials, intravenous administration of the GP IIb/IIIa inhibitor abciximab during primary PCI reduced short- and long-term mortality and reinfarction rates in patients with STEMI.\textsuperscript{6,7} Recently, experimental studies have suggested that abciximab exerts additional antiplatelet, antithrombotic, and antiinflammatory effects when local drug concentrations are higher.\textsuperscript{10} A recent study has reported that local GP IIb/IIIa receptor inhibition is higher with intracoronary administration of the GP IIb/IIIa inhibitor eptifibatide.\textsuperscript{11} Therefore, a higher local drug concentration by intracoronary administration of abciximab is expected to further improve clinical outcome. Although small- to medium-scale registries and randomized clinical trials have suggested beneficial clinical effects of intracoronary administration,\textsuperscript{12} this has not been investigated in a medium-scale randomized clinical trial with an adequate number of patients to assess myocardial reperfusion. Furthermore, there is no information at present with regard to the combined strategy of thrombus aspiration and intracoronary abciximab administration. Therefore, we investigated whether intracoronary administration of abciximab is superior to intravenous administration in improving myocardial reperfusion in STEMI patients undergoing primary PCI with thrombus aspiration.

Clinical Perspective on p \textbullet\textbullet\textbullet

Methods

Study Design and Population

The Comparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) trial was a single-center, prospective, randomized, open-label trial with blinded evaluation of end points. The detailed study design has been published previously.\textsuperscript{13} Between September 2008 and April 2010, consecutive STEMI patients undergoing primary PCI were randomly assigned to either an intracoronary or an intravenous bolus of abciximab (0.25 mg/kg body weight; ReoPro 2 mg/mL, Centocor BV, Leiden, the Netherlands). This study was performed at a high-volume university medical center providing 24-hour emergency cardiac care with 7 referral hospitals in a region of 750,000 inhabitants. The study was approved by the Medical Ethics Review Committee of the University Medical Center of Groningen. All patients gave informed consent.

All STEMI patients who were candidates for primary PCI were considered eligible for participation. STEMI was defined as chest pain suggestive of myocardial ischemia for at least 30 minutes before hospital admission, time from symptom onset of \textless 12 hours, and an ECG with new ST-segment elevation in 2 or more contiguous leads of \textgreater 0.2 mV in leads V<sub>2</sub> to V<sub>3</sub> and/or \textgreater 0.1 mV in other leads or a new-onset left bundle-branch block. Exclusion criteria were rescue PCI after thrombolytic therapy, need for emergency coronary artery bypass grafting, presence of cardiacogenic shock, a life expectancy of \textless 6 months, inability to provide informed consent, age <18 years, and contraindications for the use of abciximab, including active internal bleeding, history of stroke within 2 years, recent major surgery or trauma, intracranial neoplasm, arteriovenous malformation or aneurysm, bleeding diathesis, severe uncontrolled hypertension, thrombocytopenia, vasculitis, hypertensive or diabetic retinopathy, severe liver or kidney failure, and hypersensitivity to murine proteins.

Treatment

Patients were pretreated with aspirin (500 mg), heparin (5000 IU), and high-dose clopidogrel (600 mg), usually in the ambulance. When prasugrel became available in certain ambulances in 2010, use of prasugrel (60 mg) instead of clopidogrel was allowed. After diagnostic coronary angiography was performed, patients who met the eligibility criteria were randomized by means of sealed envelopes. After randomization, a bolus of abciximab was administered through the guiding catheter proximal to the lesion in the infarct-related artery over a period of 1 minute in patients assigned to intracoronary administration directly after first restoration of antegrade flow. The preferred initial treatment step to restore antegrade flow consisted of manual thrombus aspiration (Export Aspiration Catheter; Medtronic Inc, Santa Rosa, Calif) under continuous suction. In patients assigned to intravenous administration, abciximab was administered during PCI, but the exact timing of administration was not specified by protocol. Additional predilatation or postdilatation with a balloon and stent implantation were at the discretion of the operator. Intracoronary administration of nitroglycerine (400 \textmu g) was administered periprocedurally at the operator’s discretion. During PCI, additional low-dose weight-adjusted heparin was administered as guided by the activated clotting time (target, 200 to 250 seconds). No 12-hour infusion was initiated after PCI. Standard therapy after PCI included aspirin, clopidogrel, \textbeta-blockers, lipid-lowering agents, and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, according to current international guidelines.\textsuperscript{14}

End Points

The primary end point was the incidence of restored myocardial reperfusion, defined as complete ST-segment resolution (STR). Secondary end points of myocardial reperfusion included myocardial blush grade (MBG) and residual ST-segment deviation. Other secondary end points included incidence of Q waves, postprocedural Thrombolysis in Myocardial Infarction (TIMI) flow and angiographically visible distal embolization, enzymatic infarct size, all-cause mortality, and major adverse cardiac events (a combined end point of cardiac mortality, reinfarction, and target vessel revascularization) at 30 days. A safety end point consisted of in-hospital bleeding, defined according to the TIMI bleeding classification.\textsuperscript{15}

ECG Analysis

For evaluation of the ECG end points, a 12-lead ECG was acquired at the time of presentation and at 30 to 60 minutes after primary PCI. The magnitude of ST-segment deviation was measured 60 ms from the J point. STR was assessed by comparing the ST-segment deviation in the infarct-related area on the ECG after PCI with the ECG at presentation and was categorized as complete (\textgreater 70\%), partial (30\% to 70\%), or absent (\textless 30\%), as previously described.\textsuperscript{16} On the ECG after PCI, residual ST-segment deviation was categorized as \textless 2, 2 to 5, 5 to 10, or \textgreater 10 mm by summing the residual ST-segment deviation as previously described.\textsuperscript{17} New-onset Q waves on the ECG after PCI were defined as an initial negative deflection of the QRS complex of \textgreater 0.1 mV and \textgreater 40 ms in an ECG lead related to the myocardial area of infarction together with all pathological Q waves.\textsuperscript{18} All ECG recordings were analyzed by a physician blinded to treatment allocation and clinical data. When in doubt, the recordings were reviewed by 2 additional physicians until consensus was reached.

Angiographic Analysis

MBG was categorized as follows:\textsuperscript{19} 0 = no myocardial blush, or contrast density; 1 = minimal myocardial blush; 2 = moderate myocardial blush but less than that obtained during angiography of a contralateral or ipsilateral non–infarct-related coronary artery; and 3 = normal myocardial blush comparable to that.
obtained during angiography of a contralateral or ipsilateral non–infarct-related coronary artery. In addition, MBG was measured with the quantitative blush evaluator, which provides a computer-assisted and continuous score. TIMI flow was defined as previously described. Distal embolization after PCI was defined as a new circumscribed filling defect and/or abrupt cutoff of the vessel distal to the target lesion. Thrombus was assessed according to the criteria of the TIMI group. Coronary angiograms were analyzed by 2 physicians blinded to treatment allocation and clinical data until consensus was reached.

**Infarct Size**

Infarct size was estimated by serial measurements of cardiac markers, including creatine kinase, creatine kinase-MB, and cardiac troponin T. Blood was sampled at baseline and at 3, 6, 9, 12, 18, 24, and 48 hours after PCI in patients who were hospitalized in this center after PCI. Peak release, time to peak release, and area under the curve over the first 48 hours were determined. If patients were observed for shorter periods, the area under the curve was estimated by multiplying the time-averaged mean level by 48 hours (adjusted values).

**Clinical Follow-Up**

Clinical follow-up was obtained from the central personal records database, hospital records, and interviews with the patients and/or their general practitioners. Mortality was considered cardiac unless an unequivocal noncardiac cause of death was established. Reinforcement was defined as recurrent symptoms suggestive of ischemia with new ST-segment elevation and/or elevation of the levels of cardiac markers. Target vessel revascularization was defined as ischemia-driven revascularization of the infarct-related artery with PCI or coronary artery bypass grafting. Clinical events were adjudicated by a committee consisting of 3 physicians blinded to treatment allocation.

**Sample Size and Statistical Analysis**

In previously published data, complete STR was achieved in 56.6% of STEMI patients treated with thrombus aspiration. To detect a 25% increase in the incidence of this primary end point in patients randomized to the intracoronary group, a total of 530 patients were required to achieve 90% power at a 5% significance level (2 sided), allowing 10% of ECGs to be not assessable for the primary end point. Statistical analyses were performed by intention to treat. Statistical significance was considered at a 2-tailed level (2 sided), allowing 10% of ECGs to be not assessable for the primary end point. Differences between group means were assessed with the 2-tailed Student t test or Mann-Whitney U test if samples were not normally distributed. The \( \chi^2 \) or Fisher exact test was used to test differences between proportions. Statistical analyses were performed with the Statistical Package for the Social Sciences version 16.0.2 (SPSS Inc, Chicago, Ill). Investigators had full access to all primary data.

**Results**

A total of 534 STEMI patients were randomly assigned to either intracoronary (n = 271) or intravenous (n = 263) abciximab administration (Figure 1). A total of 80 patients were excluded because of a contraindication for the use of abciximab (n = 38), an inability to provide informed consent (n = 2), cardiogenic shock (n = 38), and need for emergency coronary artery bypass grafting (n = 2). Baseline characteristics did not differ significantly between patients randomized to intracoronary or intravenous administration (Table 1). Clopidogrel was administered routinely before PCI in the prehospital setting either in the ambulance or at the referral hospital. In patients admitted through the emergency department (9%), clopidogrel was administered before transportation for PCI. In 3%, prasugrel was administered after PCI. Prasugrel was administered instead of clopidogrel in 2 patients randomized to intracoronary administration and 4 randomized to intravenous administration. Abciximab was administered after a median time of 3 minutes (interquartile range [IQR], 2 to 5 minutes) in the intracoronary group and 1 minute (IQR, 0–3 minutes) in the intravenous group from first intracoronary intervention \( (P<0.001) \). Crossovers occurred nonintentionally in 3 patients randomized to intracoronary administration.

**ECG End Points**

The primary end point of complete STR was achieved in 64% of the intracoronary group and 62% of the intravenous group \( (P=0.562) \). STR could not be assessed in 20 of 271 patients (7.4%) in the intracoronary group and 26 of 263 patients (9.9%) of the intravenous group \( (P=0.302) \) because no pre-PCI ECG was available (n = 11), no post-PCI ECG was available (n = 24), or conduction abnormal-
Table 1. Baseline Characteristics of the 534 Patients Randomized to Intracoronary or Intravenous Administration of Abciximab

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary (n=271)</th>
<th>Intravenous (n=263)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>64±13</td>
<td>64±13</td>
<td>0.940</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>208/271 (77)</td>
<td>187/263 (71)</td>
<td>0.137</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>119/270 (44)</td>
<td>129/263 (49)</td>
<td>0.250</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>80/268 (30)</td>
<td>74/261 (28)</td>
<td>0.705</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>36/271 (13)</td>
<td>29/263 (11)</td>
<td>0.425</td>
</tr>
<tr>
<td>Family history, n (%)</td>
<td>125/267 (47)</td>
<td>124/262 (47)</td>
<td>0.906</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>116/270 (43)</td>
<td>127/263 (48)</td>
<td>0.217</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>6/271 (2)</td>
<td>5/263 (2)</td>
<td>0.799</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>25/271 (9)</td>
<td>21/263 (8)</td>
<td>0.619</td>
</tr>
<tr>
<td>Previous CABG, n (%)</td>
<td>6/271 (2)</td>
<td>5/263 (2)</td>
<td>0.774</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>11/270 (4)</td>
<td>12/262 (5)</td>
<td>0.774</td>
</tr>
<tr>
<td>Preinfarction angina, n (%)</td>
<td>73/270 (27)</td>
<td>76/263 (29)</td>
<td>0.632</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27±4</td>
<td>27±5</td>
<td>0.929</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>131±27</td>
<td>129±25</td>
<td>0.319</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>76±15</td>
<td>74±13</td>
<td>0.231</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>76±20</td>
<td>78±18</td>
<td>0.196</td>
</tr>
<tr>
<td>Ischemic time, median (IQR), min</td>
<td>180 (120–275)</td>
<td>179 (128–275)</td>
<td>0.567</td>
</tr>
<tr>
<td><strong>Angiographic, n (%)</strong></td>
<td></td>
<td></td>
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<tr>
<td>No. of diseased vessels</td>
<td></td>
<td></td>
<td>0.295</td>
</tr>
<tr>
<td>1</td>
<td>123/271 (45)</td>
<td>101/261 (39)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>78/271 (29)</td>
<td>84/261 (32)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>70/271 (26)</td>
<td>76/261 (29)</td>
<td></td>
</tr>
<tr>
<td>Infarct-related artery</td>
<td></td>
<td></td>
<td>0.844</td>
</tr>
<tr>
<td>LAD</td>
<td>121/271 (45)</td>
<td>124/263 (47)</td>
<td></td>
</tr>
<tr>
<td>Cx</td>
<td>33/271 (12)</td>
<td>34/263 (13)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>112/271 (41)</td>
<td>99/263 (36)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5/271 (2)</td>
<td>6/263 (2)</td>
<td></td>
</tr>
<tr>
<td>TIMI flow grade, n (%)</td>
<td></td>
<td></td>
<td>0.050</td>
</tr>
<tr>
<td>0</td>
<td>125/271 (46)</td>
<td>145/263 (55)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>25/271 (9)</td>
<td>31/263 (12)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>64/271 (24)</td>
<td>49/263 (19)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>57/271 (21)</td>
<td>38/263 (14)</td>
<td></td>
</tr>
<tr>
<td>Thrombus present, n (%)</td>
<td>236/270 (87)</td>
<td>242/263 (92)</td>
<td>0.080</td>
</tr>
<tr>
<td>Collaterals present, n (%)</td>
<td>52/266 (20)</td>
<td>48/256 (19)</td>
<td>0.817</td>
</tr>
<tr>
<td><strong>Procedural, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>266/271 (98)</td>
<td>255/263 (97)</td>
<td>0.370</td>
</tr>
<tr>
<td>Balloon predilatation</td>
<td>119/271 (44)</td>
<td>126/263 (48)</td>
<td>0.354</td>
</tr>
<tr>
<td>Stent implantation</td>
<td>256/271 (95)</td>
<td>251/263 (95)</td>
<td>0.608</td>
</tr>
<tr>
<td>Postdilatation</td>
<td>32/271 (12)</td>
<td>25/263 (10)</td>
<td>0.389</td>
</tr>
<tr>
<td>IABP use</td>
<td>11/271 (4)</td>
<td>16/263 (6)</td>
<td>0.286</td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; BMI, body mass index; IQR, interquartile range; LAD, left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; and IABP, intra-aortic balloon pumping. Data are presented as mean±SD or No./total No. (%) as appropriate.

Ities or arrhythmias were seen on the ECG (n=11). Patients without primary end-point analysis were slightly older, had a longer ischemic time, and more often had hypercholesterolemia, multivessel disease, and the left main, graft, or right coronary artery as the infarct-related artery. Concordantly, there were no differences in the distributions of residual ST-segment deviation between the intracoronary and intravenous groups (P=0.662; Figure 2). The incidence and number of Q waves on the postprocedural ECG were similar in both groups (77% versus 82%; P=0.143; median, 2 [IQR, 1 to 3] versus 2 [IQR, 1 to 4]; P=0.114). The median time from abciximab administration to the ECG after PCI was 4 minutes shorter for the intracoronary than for the intravenous group (38 minutes [IQR, 31 to 49 minutes] versus 42 minutes [IQR, 33 to 74 minutes]; P<0.001).

### Angiographic End Points

Coronary angiograms were assessable in 526 of 534 patients (99%). In contrast to the distribution of ECG end points, the distribution of MBG was borderline significant in favor of patients randomized to intracoronary administration (P=0.052; Figure 2). Moreover, the incidence of MBG 2/3 was significantly higher in the intracoronary than in the intravenous group (76% versus 67%; P=0.022). When measured quantitatively with the quantitative blush evaluator (available in 75% of patients), myocardial reperfusion was slightly better in the intracoronary group than in the intravenous group, but this was not statistically significant (10.1±3.5 versus 9.7±3.6; P=0.269). After thrombus aspiration, assessable in 90% of patients, flow was restored (TIMI grade 3) in 211 of 235 patients (90%) in the intracoronary group and 201 of 232 patients (87%) in the intravenous group (P=0.291). Postprocedural TIMI grade 3 flow was achieved in 89% and 86% of the intracoronary and intravenous groups, respectively (P=0.261). Postprocedural distal embolization occurred at similar frequencies between both groups (12% and 13%, respectively; P=0.635). The median time from abciximab administration to the angiographic run containing the blush sequence was 1 minute shorter for the intracoronary than for the intravenous group (8 minutes [IQR, 5 to 12 minutes] versus 9 minutes [IQR, 6 to 15 minutes]; P=0.006).

### Infarct Size

Data on enzymatic infarct size could be assessed in 248 of 534 patients (46%). Infarct size was ~30% smaller in the intracoronary group than in the intravenous group (1214 U/L [IQR, 488 to 2184 U/L] versus 1746 U/L [IQR, 733 to 3383 U/L] for creatinine kinase, P=0.008; 154 U/L [IQR, 62 to 262 U/L] versus 232 U/L [IQR, 90 to 400 U/L] for creatinine kinase-MB, P=0.003; and 3.03 µg/L [IQR, 0.95 to 5.81 µg/L] versus 4.36 µg/L [IQR, 1.43 to 8.56 µg/L] for cardiac troponin T, P=0.008; Table 2).

### Clinical Follow-Up

In total, 12 patients (2.2%) died within 30 days. All-cause mortality was 1.8% and 2.7% in the intracoronary and intravenous groups, respectively (P=0.524; Table 3).
incidence of major adverse cardiac events was low and not significantly different between the 2 groups (5.5% in the intracoronary group versus 6.1% in the intravenous group; \( P = 0.786 \)).

**Safety**

There were no adverse procedural events related to intracoronary abciximab administration. The incidence of in-hospital major and minor bleeding was low and similar between the intracoronary and intravenous groups (for major bleeding, 3.7% versus 3.4%, \( P = 0.867 \); for minor bleeding, 7.7% versus 6.8%, \( P = 0.688 \)). In-hospital thrombocytopenia \( <150 \times 10^9/\text{L} \) developed in patients randomized to intracoronary and intravenous administration at similar frequencies (12% versus 13%; \( P = 0.794 \)).

**Discussion**

This study indicates that intracoronary administration of the GP IIb/IIIa inhibitor abciximab during primary PCI with thrombus aspiration compared with intravenous administration does not improve myocardial reperfusion as assessed by STR. However, intracoronary administration is similar frequencies (12% versus 13%; \( P = 0.794 \)).

**Table 2. Enzymatic Infarct Size in Patients With Complete In-Hospital Follow-Up**

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary (n=126)</th>
<th>Intravenous (n=122)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak CK, U/L</td>
<td>1214 (488–2184)</td>
<td>1746 (733–3383)</td>
<td>0.008</td>
</tr>
<tr>
<td>Peak CK-MB, U/L</td>
<td>154 (62–262)</td>
<td>232 (90–400)</td>
<td>0.003</td>
</tr>
<tr>
<td>Peak cTnT, μg/L</td>
<td>3.03 (0.95–5.81)</td>
<td>4.36 (1.43–8.56)</td>
<td>0.008</td>
</tr>
<tr>
<td>Time to peak CK, h</td>
<td>7 (5–11)</td>
<td>8 (5–11)</td>
<td>0.991</td>
</tr>
<tr>
<td>Time to peak CK-MB, h</td>
<td>6 (5–9)</td>
<td>6 (5–9)</td>
<td>0.926</td>
</tr>
<tr>
<td>Time to peak cTnT, h</td>
<td>9 (6–13)</td>
<td>9 (6–12)</td>
<td>0.924</td>
</tr>
<tr>
<td>AUC48 CK</td>
<td>1134 (474–1886)</td>
<td>1571 (612–2597)</td>
<td>0.023</td>
</tr>
<tr>
<td>AUC48 CK-MB</td>
<td>117 (56–219)</td>
<td>171 (80–277)</td>
<td>0.006</td>
</tr>
<tr>
<td>AUC48 cTnT</td>
<td>2.92 (0.87–5.35)</td>
<td>3.31 (1.39–8.23)</td>
<td>0.032</td>
</tr>
<tr>
<td>AUC48 CK adjusted</td>
<td>1463 (600–2841)</td>
<td>2206 (1002–3781)</td>
<td>0.008</td>
</tr>
<tr>
<td>AUC48 CK-MB adjusted</td>
<td>172 (82–305)</td>
<td>296 (122–440)</td>
<td>0.001</td>
</tr>
<tr>
<td>AUC48 cTnT adjusted</td>
<td>4.00 (1.36–7.41)</td>
<td>6.22 (2.08–12.03)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

CK indicates creatinine kinase; cTnT, cardiac troponin T; and AUC, area under the curve. Data are presented as median (interquartile range).

**Table 3. Clinical Outcome at 30 Days in Patients Randomized to Intracoronary or Intravenous Administration of Abciximab**

<table>
<thead>
<tr>
<th></th>
<th>Intracoronary (n=271), n (%)</th>
<th>Intravenous (n=263), n (%)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>5 (1.8)</td>
<td>7 (2.7)</td>
<td>0.524</td>
</tr>
<tr>
<td>Cardiac mortality</td>
<td>4 (1.5)</td>
<td>6 (2.3)</td>
<td>0.492</td>
</tr>
<tr>
<td>TVR</td>
<td>9 (3.3)</td>
<td>10 (3.8)</td>
<td>0.764</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>3 (1.1)</td>
<td>4 (1.5)</td>
<td>0.721</td>
</tr>
<tr>
<td>IST</td>
<td>1 (0.4)</td>
<td>3 (1.1)</td>
<td>0.366</td>
</tr>
<tr>
<td>MACEs</td>
<td>15 (5.5)</td>
<td>16 (6.1)</td>
<td>0.786</td>
</tr>
</tbody>
</table>

TVR indicates target vessel revascularization; IST, in-stent thrombosis; and MACEs, major adverse cardiac events.
related to improved myocardial reperfusion as assessed by MBG, as well as in the subset of patients with evaluable infarct size, to a 30% smaller enzymatic infarct size. The CICERO trial is the largest clinical trial to date to determine the effect of intracoronary versus intravenous administration of abciximab in STEMI patients undergoing primary PCI. Moreover, this is the first medium-scale trial performed in a contemporary cohort of STEMI patients who were treated with manual thrombus aspiration.

Abciximab acts as a potent inhibitor of platelet aggregation mainly by competitively binding to the GP IIb/IIIa receptor on the surface of activated human platelets. As a result of a higher affinity to this receptor, abciximab prevents binding of fibrinogen and von Willebrand factor to activated platelets, blocking the final common pathway for platelet aggregation.10 Experimental studies have suggested that abciximab has additional dose-dependent antiplatelet, antithrombotic, and antiinflammatory features. Abciximab not only prevents platelet aggregation in vitro but also promotes thrombus disaggregation.10 These findings suggest that a higher local concentration, achieved by intracoronary administration, results in improved outcome. Several small-scale studies have reported improved myocardial salvage, left ventricular functional recovery, and a smaller infarct size after intracoronary administration of abciximab.12 In a randomized trial in 154 patients by Thiele et al,25 STR as a continuous measure was higher in the intracoronary than in the intravenous group (77.8% versus 70.0%). However, this positive study was powered to detect differences in infarct size and extent of microvascular obstruction by MRI. In the present study, which was powered to detect a clinically relevant improvement in STR, we could not confirm the positive findings as previously suggested. In contrast, we did observe a clinically relevant improvement in myocardial reperfusion as assessed by MBG and, in the subset of patient with evaluable enzymatic infarct size, a reduction in infarct size in patients randomized to intracoronary administration, which are consistent with the effects reported previously.25 Furthermore, the magnitude of the effect observed in this study was comparable.

Can the neutral findings on our primary end point be explained by differences between this and previous studies? In the positive study by Thiele et al,25 the patient population appeared to be at a higher clinical risk than in our study: patients presented with an 60-minute-longer ischemic time and a higher incidence of TIMI grade 0/1 flow, diabetes mellitus, and anterior infarction. In subgroup analysis, the benefit was observed in patients treated after 4 hours of symptom onset. Furthermore, high-dose clopidogrel preloading was performed in a small proportion of patients, and the use of thrombus aspiration was not reported. Our patient population resembled a recent neutral study with a similar baseline risk, including similar ischemic time, frequent use of clopidogrel preloading, and use of thrombus aspiration in 40%.26 Therefore, it is possible that the benefit of intracoronary administration on myocardial reperfusion was offset by a lower clinical risk and the routine use of thrombus aspiration in the present study.

The actual incidence of STR was higher than the estimated incidence used for sample size estimation. This estimation was based on data from the Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction (TAPAS) study performed in our center, which showed complete STR in 56.6% of patients randomized to thrombus aspiration.8 In a more recent trial, ADenosine Administration during and after Primary percutaneous coronary intervention in acute myocardial infarction Trial (ADAPT), however, the rate of complete STR was considerably higher (66.5%) and more similar to that in this study.17 It is therefore likely that the higher rate of STR is explained by differences in the rate of actual thrombus aspiration: TAPAS patients randomized to thrombus aspiration underwent thrombus aspiration in 84%, whereas 95% of patients in the ADAPT control group and 97% of CICERO patients underwent thrombus aspiration. Because the more recent STR data were not available during the design of CICERO, we could base our assumptions only on the TAPAS data. During the years after TAPAS, no significant changes took place that could explain the higher rates of STR.

We report an unexpected discrepancy between myocardial reperfusion as assessed by STR and by MBG; they are usually consistent in both positive and negative studies and in previous studies reporting on intracoronary abciximab.8,17,25 Several reasons may account for this discrepancy. One possible reason is that STR and MBG represent different pathophysiological phenomena. MBG reflects mechanical patency of the microvasculature, whereas STR may reflect the functional status of the myocardial cells.27 Although both markers are widely accepted as surrogate end points of clinical outcome,16,19,28 restoration of myocardial reperfusion as defined by complete STR or MBG 2/3 is discordant in approximately one third of STEMI patients.19,29 Nevertheless, both markers are of independent prognostic value in predicting long-term mortality.16,19,28,30 Recently, however, the prognostic value of STR has been debated in patients treated with primary PCI.31 This discrepancy between both markers cannot be explained by the findings in this study and deserves further investigation. A second possible reason is that both markers are assessed at different time points after primary PCI: MBG directly after PCI and STR at 30 to 60 minutes after PCI. The beneficial effect of intracoronary administration on myocardial reperfusion may be present directly after PCI but not at 30 to 60 minutes after PCI. A discrepancy between myocardial reperfusion outcomes immediately after PCI and compared with later after PCI has been reported previously.32 A third possible reason is that intracoronary administration itself instead of abciximab improves myocardial reperfusion directly after PCI but negates it during the first hour after PCI. Although there was no control group with intracoronary injection of saline, it is not likely that intracoronary administration itself would also result in the relevant reduction in enzymatic infarct size that was also observed in this study.

In contrast to previous studies that have suggested reductions to >50% of the incidence of major adverse cardiac events at 30 days in patients randomized to
intracoronary administration, we found no reduction or trend toward reduction. First of all, this study had insufficient power to detect differences in clinical events. Furthermore, this study was performed in patients receiving contemporary treatment, including prehospital administration of high-dose clopidogrel and thrombus aspiration. The absolute number of clinical events at 30 days was much lower in this trial than in these previous studies, making it even less likely to come to statistically significant improvements.

Although we observed conflicting results on myocardial reperfusion, the potential beneficial effects of intracoronary administration may become evident after 30 days. The reduction in enzymatic infarct size observed in a subset of patients may well translate into a better recovery of left ventricular function and improved clinical outcome at longer follow-up. Because this study was underpowered to detect possible differences in clinical events, larger randomized multicenter trials are needed to evaluate whether intracoronary administration during primary PCI improves clinical outcome. This is being investigated in an ongoing trial. In addition, local delivery of abciximab with a dedicated infusion catheter is currently being investigated in 2 trials that randomize STEMI patients to intracoronary bolus versus intravenous bolus (IC-ClearLy) and to intracoronary versus no bolus with or without thrombus aspiration in patients treated with bivalirudin (INFUSE AMI; http://www.ClinicalTrials.gov; unique identifier, NCT00976521).

Limitations
First, we performed an open-label study because blinding of the operator was not feasible. However, all end points were assessed in a blinded manner. Second, this study was powered on STR instead of a clinical end point. However, STR is strongly related to clinical outcomes and therefore is widely accepted as a surrogate marker. In addition, STR was measured in this study only as a categorization into 3 groups, thereby preventing direct comparison between this study and previous studies reporting on continuous STR. In general, categorization makes a measurement less sensitive to treatment differences. However, STR categorized into 3 groups is frequently used in medium-scale interventional trials to detect a clinically relevant improvement in STR. Third, we analyzed enzymatic infarct size in the subset of patients who were hospitalized in this center after PCI. However, the choice to stay in this center was based on geographical reasons and not biased by randomization. Fourth, all patients in this study received abciximab in a bolus-only strategy, which is not currently recommended. Bolus-only use is supported by studies showing that bolus-only use reduces bleeding complications and is not inferior to abciximab bolus with subsequent 12-hour infusion in stable and moderate- to high-risk patients with acute coronary syndromes. In this study, we did not compare the bolus-only strategy with the standard bolus with subsequent 12-hour infusion strategy. However, because infusion was not initiated in either randomization group, it has not influenced our comparison of intracoronary and intravenous administration. Finally, we did not investigate the effect of timing of intracoronary administration. Although previous studies have reported on intracoronary administration after wire passage but before restoration of epicardial flow, we chose to perform intracoronary administration after restoration of flow to have an optimal local concentration through the coronary artery both at the culprit site and in the distal microvasculature.

Conclusions
In STEMI patients undergoing primary PCI with thrombus aspiration, intracoronary administration of abciximab is not superior to intravenous administration in improving myocardial reperfusion assessed by STR as the primary end point. However, intracoronary administration is associated with improved myocardial reperfusion as assessed by MBG and, in the subset of patients with evaluable infarct size, a smaller enzymatic infarct size. Larger randomized multicenter trials are required to evaluate whether intracoronary administration reduces clinical adverse events.

Acknowledgments
The authors thank the staff of the catheterization laboratory and coronary care unit and Wybe Nieuwland, MD, PhD, for their contributions in the acute care setting and Karim D.E. Mahmoud, BSc, and Margriet Couperus for their assistance in data collection.

Disclosures
None.

References


**CLINICAL PERSPECTIVE**

Administration of the glycoprotein IIb/IIIa inhibitor abciximab is an effective adjunctive antiplatelet strategy during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Experimental studies have reported that higher local concentrations of abciximab exert additional effects, including disaggregation of newly formed thrombus, and can be achieved by intracoronary administration. Recently, small-scale studies have suggested beneficial clinical effects of intracoronary over intravenous administration. In the present Comparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) trial, 534 ST-segment elevation myocardial infarction patients were randomized within 12 hours of symptom onset to either an intracoronary or an intravenous bolus of abciximab during primary percutaneous coronary intervention with thrombus aspiration. Patients were pretreated with aspirin, heparin, and high-dose clopidogrel. Intracoronary administration of abciximab compared with intravenous administration did not improve the rate of successful myocardial reperfusion as assessed by ST-segment resolution. In contrast, intracoronary administration was associated with a significantly higher rate of successful myocardial reperfusion as assessed by myocardial blush grade and a smaller enzymatic infarct size. In addition, bleeding complications occurred at similar frequencies between both treatment groups. Although intracoronary administration did not improve the primary end point of ST-segment resolution, the beneficial effects on secondary end points may translate into improved clinical outcome. Larger randomized multicenter trials are required to investigate whether intracoronary administration of abciximab reduces major adverse cardiac events.
Intracoronary Versus Intravenous Administration of Abciximab in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention With Thrombus Aspiration: The Comparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction (CICERO) Trial


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Primary PCI 시행 시 관상동맥 내 Abciximab 투여가 정맥 투여보다 낫다.

조상 호 교수 한림대학교 부심생성 순환기의과

Summary

배경
Glycoprotein IIb/IIIa inhibitor인 abciximab의 투여는 ST분절 상승 급성 심근경색(ST-segment elevation myocardial infarction, STEMI)의 치료에 입차 관상동맥 중재술(primary percutaneous coronary intervention, primary PCI)의 효과적인 보조 역할로 알려져 있다. 소규모 연구에서는 관상동맥 내(intracoronary, IC)로 abciximab를 투여하는 것이 정맥 투여보다 더 효과적이라고 보고하고 있으나, 중간 정도 규모의 무작위 임상연구에서 증명된 바는 없다.

방법 및 결과
증상 발생 후 12시간 이내에 primary PCI와 혈관개방술(thrombus aspiration)을 시행받은 중 534명의 STEMI 환자를 대상으로 abciximab(0.25mg/kg)를 IC 혹은 정맥주사(intravenous, IV)로 투여하였고, 두군의 대조군은 무작위로 배정하였다. 모든 환자는 이하파인 화이트군, 클로피드로글락탈지프로를 받았다. 입상 임상결과는 완전한 ST분절의 정상화(기저치보다 70% 이상 하강)로 정의되는 심근판류의 회복이다. 이는 임상결과 myocardial blush grade, 심근 효소로 정의한 경색의 크기 30일치 주요 심혈관 사건의 발생이다. 완전한 ST분절의 정상화는 IV 군에서 동일하나, abciximab 투여군 64% vs. 62% (P=0.562), 심근 효소의 지표인 myocardial blush grade 2/3의 원도는 IC군이 IV군보다 더 높았다(36% vs. 67%, P<0.022). 심근 효소로 평판한 경우 크게 IC군에서 더 작았다(P=0.008, 심혈관 사건 발생은 양 군에서 비슷하였다(5.5% vs. 6.1%, P=0.786).

결론
Primary PCI와 thrombus aspiration을 시행받은 STEMI 환자에서 abciximab의 IC 투여가 IV 투여보다 ST분절의 정상화 homosexuality에서는 유리하지 않으나, myocardial blush grade로 측정한 심근의 재판류 정도의 심근 효소로 측정한 경색 크기에서는 더 우수한 효과를 보였다.
기계적인 manual thrombus aspiration과 보조 약물 치료인 glycoprotein IIb/IIIa inhibitor(GPⅡb/IIIa)의 사용이 STEMI 환자의 primary PCI 시에 심근관류 액체를 얻는 기여를 하였습니다. abciximab의 IC 두어가 IV 두어보다 이점이 많았다고도 하였습니다. 연구가 보고된 이후 실제 임상에서 많이 사용되고 있으나 두 가지를 병합한 치료가 좀 더 많이 환자를 대상으로 더 IV GP를 비교한 연구는 없다. 이에 본 연구는 각 군의 250여 명씩 배치하여 모든 환자에게 aspiration catheter를 이용한 thrombus aspiration을 시행한 후, IC 대 IV abciximab의 효과를 평가하였다. 

1. 임상적 조사
   1.1. 대상
   당뇨병과 심장병의 경상화(primary PCI 30-60분 후의 심장병에서 ST 70% 이상 감소한 경우)를 진단한 환자. 일상적인 발생 및 myocardial blush grade, 경계 크기는 이차 목표였다.
   1.2. 방법
   1.2.1. abciximab은 심근관류를 평가한 심근관류의 30일 이상 임상시험에서는 두 투여방 식별되지 않았으나, myocardial blush grade, 심근 조절의 체질학적 경계의 크기 감소에서 IC abciximab의 효과가 두배가 더 효과적이었다. IC 직관적 조절적 abciximab 본 실험장이 더 큰 antplatelet, antithrombotic, anti-inflammatory 효과를 발휘한다는 실험적 연구 결과를 임상적으로 탐명하는 증거가 될 수 있다.

2008년 Circulation에 실린 유사한 연구에서는 심근관류를 통한 응급심장시술에서 IC군에서 좋은 경보를 보였는데 2.2% vs. 15.6%, P=0.06, relative risk 0.33, 95% CI 0.09-1.03, 이런 연구에서는 5.5% 대 6.1%로 두 군에서 차이가 있었다.

비교 두 연구를 직접 비교하는 것은 무리가 있었지만, 홍미롭게도 IC 두어군의 심장관류 발생률은 두 연구에서 비슷한 비율이었다. 이 연구에 IV 두어군의 심장관락 발생률이 6.1%로, 이전 연구의 25.6%보다 활동성이 낮은 발생률을 보였다. 두 연구의 차이는 thrombus aspiration 여부(이전 연구에서는 양 군 모두 시행) 및 abciximab의 12시간 지속 두어 여부(이전 연구에서 양 군 모두 시행) 및 그외의 참가자 이전 연구에서 더 많았다는 TIMI 0-1 flow의 비율이 높고, 나머진 전 혈관 기간 이 길며 뒤로 나온 LAD 분리가 많음도 있었다.

이를 해석하면, 오히려 thrombus aspiration이 12시간 abciximab 지속 두어보다 유리할 수 있으며, IV abciximab bolus thrombus aspiration을 한다면 관리의 부분이 증가할 수 있는 abciximab의 추가 지속 정주가 필요하지 않을 수도 있을 것이다. 또한, 두 연구에서 IC abciximab bolus thrombus aspiration과 IC abciximab bolus recombinant 지속 정주가 심혈관 사건 발생에 차이가 없었으므로 IC 두어 사태에는 thrombus aspiration이나 abciximab 지속 정주 중 유리한 방법으로 한 가지를 선택해 시행하는 것이 좋을 것이다. 개인적으로는 경종 부분의 가능성이 있으며 bolus abciximab 지속 정주로는 primary PCI 당시 IC abciximab bolus thrombus aspiration을 시행하여 thrombus burden을 줄여주며 동시에 abciximab 지속 정주를 끼치게 하는 것이 더 나을 것으로 생각한다.

이러한 여러 가능성을 실제로 동정하기 위해서는 일부 abciximab IC 대 IV의 thrombus aspiration 여부 2x2 배정으로 임상시험 발생율을 연구 목표로 삼는다. 규모 연구가 진행되어야 할 것이다.
Primary PCI 시행 시 관상동맥 내 Abciximab 투여가 정맥 투여보다 낫다.

조상 호 교수 한강대학교 동식병원 순환기내과

Summary

배경
Glycoprotein IIb/IIIa inhibitor인 abciximab의 투여는 ST분절 상승 급성 심근경색(ST-segment elevation myocardial infarction, STEMI)의 치료의 일차 관상동맥 재단백(primary percutaneous coronary intervention, primary PCI)의 효과적인 보조 약물치료로 알려져 있다. 소규모 연구에서는 관상동맥 내(intracoronary, IC)로 abciximab을 투여하는 것이 정맥 투여보다 더 효과적이라고 보고하고 있으나, 중견 정도 규모의 무작위 임상연구에서 증명된 바는 없다.

방법 및 결과
종상 발생 후 12시간 이내에 primary PCI와 혈관내유전 (thrombus aspiration)을 시행한 중 534명의 STEMI 환자를 대상으로 abciximab(0.25mg/kg)을 IC, 혹은 정맥에서(intravenous, IV)로 두어 비교한 군으로 무작위 배정 하였다. 모든 환자는 아스피린, 아스피린, 클로피도그릴, 덩굴치료를 받았다. 일자 목표점은 완전한 ST분절의 정상화(기저보다 70% 이상 하강)로 정의되는 심근관류의 회복이다. 이차 목표점은 myocardial blush grade, 심근 호소로 평가한 양의 크기 30일지 주요 심혈관계 사건의 발생이다. 완전한 ST분절의 정상화는 IC군에서 동일하였으나(64% vs. 62%, P<0.562), 좋은 심근관류의 지표인 myocardial blush grade 2/3의 비도는 IC군이 IV군보다 더 높았었다(76% vs. 67%, P<0.022). 심근 효소로 측정한 경색 크기도 IC군에서 더 작았다(P<0.008). 심혈관계 사건 발생은 양 군에서 비슷하였다(5.5% vs. 6.1%, P=0.786).

결론
Primary PCI와 thrombus aspiration을 시행한 STEMI 환자에서 abciximab의 IC 투여가 IV 투여보다 ST분절의 정상화에서는 유리하지 않으나, myocardial blush grade로 측정한 심근의 재판류 정도의 심근 효소로 측정한 양의 크기에서의 더 우수한 효과를 보였다.
기계적인 manual thrombus aspiration과 비교 역할을 차지한 glycoprotein IIb/IIIa inhibitor(GP)의 사용이 STEMI 환자의 primary PCI 시의 심근경화에 해를 야기하기, abciximab의 IC 두어는 IV 두어보다 약간 긴 편이다. 각각의 연구가 보고된 이후 실제 임상에서 많이 사용되고 있으나 두 가지를 병렬한 자료 및 좀 더 많은 환자를 대상으로 하여 IV GP를 비교한 연구는 없다. 이에 본 연구는 각 군에 250명씩 랜덤배정하여 모든 환자에게 aspiration catheter를 이용한 thrombus aspiration을 시행한 후, ICD 4T abciximab의 효과를 평가하였다. 

본 연구는 심전도의 ST분절의 정상화(primary PCI 30분 후에 정상한 ST), 70% 이상 감소한 경우를 정의하였고, 임상적 증상 발생 및 myocardial blush grade, 경색 크기는 이차 목표였었다. 

결과는 ST분절 정상화의 경우 70%의 의한 심근관류의 30일째 심장사진시에는 두 투여군 간에 차이가 없었으나, myocardial blush grade, 심근 호소도 측정한 경색 크기 감소에서 ic abciximab이 더 효과적이다. 이는 최근의 국소적인 abciximab 높은 성공률에 큰 antplatelet, antithrombotic, anti-inflammatory 효과를 발휘하는 신경이 연구 결과를 일기적으로 높여진다는 증가가 있을 수 있다. 

2008년 Circulation에 실린 유사한 연구에서는 심근관류는 물론 임상시에는 IC군에서 좋은 경향을 보였는데, 2.2% vs. 2.6%, P<0.05, relative risk, 0.33, 95% CI, 0.09-1.90, 이반 연구에서는 5.5% 대 6.1% 두 군에서 차이가 있었다. 

비교 두 연구를 직접 비교하는 것은 무리가 있었지만, 참고로도 IC 두어군의 심장군사 발생률은 두 연구에서 비슷한 범위였다. 이번 연구는 IV 두어군의 심장군 사 발생률이 6.1%로, 이반 연구의 35.6%보다 감소된 탓이 낮은 발생률을 보였다. 두 연구의 차이는 thrombus aspiration 여부(이반 연구에서는 양 군 모두 시행, abciximab의 12시간 지속 두어 여부(이반 연구에서 양 군 모두 사용) 및 그 외의 환자와 연구에서 더 많았다는 TIMI 0.1 flow의 비율이 높고, 나머지 투여군 간에 차이가 많지 않았고 LAD 범위가 많았다. 

이를 해석하면, 오히려 thrombus aspiration이 12시간 abciximab 지속 두어보다 유의한 ICD 4T abciximab을 bolus thrombus aspiration을 한다면 군은 증상의 주요인과 증강을ующ abciximab의 추가 지속 두어가 필요하지 않을 수도 있을 것이다. 또한, 두 연구에서 IC 12시간 abciximab bolus thrombus aspiration과 IC abciximab bolus abciximab 지속 두어가 심혈관 사 건 발생에 차이가 없었으므로 IC 두어 시에는 thrombus aspiration이나 abciximab 지속 두어를 유리한 방안으로 한 가지를 선행하여 시행하는 것이 좋은 전략일 수 있고, 개인적으로는 종합적 원칙의 가능성이 있으며, 장래의 abciximab 지속 두어가 primary PCI 시에 IC abciximab bolus thrombus aspiration을 시행하여 thrombus burden을 최소화할 수 있으므로 abciximab 지속 두어를 고려해 보는 것이 더 나을 것으로 생각한다. 

이러한 여러 가능성들을 실제로 증명하기 위해서는 일부 abciximab IC 두어에 thrombus aspiration 여부를 비교하여 임상사례 발생률을 연구 목표로 삼는다. 

Reference
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