Selective Intracoronary Thrombolysis in Acute Myocardial Infarction and Unstable Angina Pectoris

P. Rentrop, M.D., H. Blanke, M.D., K. R. Karsch, M.D., H. Kaiser, M.D., H. Köstinger, M.D., and K. Leitz, M.D.

SUMMARY Streptokinase was infused into the ischemia-related coronary artery at a rate of 1000–2000 U/min for 15–95 minutes in 29 patients with acute myocardial infarction (AMI group) and in five patients with unstable angina pectoris (UAP group). Reopening of the completely obstructed vessel or increase of diameter at the site of subtotal lesions occurred in 22 AMI patients within 15–90 minutes of streptokinase infusion. In four of these patients, antegrade flow to the distal segments of the infarct vessel was seen after intracoronary nitroglycerin or sublingual nifedipine administration, which preceded streptokinase infusion, and in two patients, streptokinase infusion was combined with recanalization by means of a guide wire. Chest pain was alleviated after reperfusion; ejection fraction was 50.5 ± 12% before and 54.6 ± 9% immediately after successful intracoronary lysis (p < 0.05). Repeat angiography, performed 25 ± 11 days after the acute intervention in 19 AMI patients, revealed reocclusion of the infarct vessel in one patient. Aortocoronary bypass surgery was performed electively in six AMI patients at varying intervals after successful lysis. Upon intraoperative inspection, the bulk of myocardium perfused by the recanalized vessel was found to be viable.

Intracoronary streptokinase infusion did not result in opening the complete obstruction or improvement of lumen at the site of subtotal lesions in seven AMI patients and in all UAP patients. The total dose of 128,000 ± 36,000 U of streptokinase resulted in only minor decrease of fibrinogen, from 451 ± 93 mg% to 430 ± 91 mg%. Bleeding from the arterial puncture site in two patients, the only complications that could be attributed to the procedure, was due to heparinization.

Intracoronary streptokinase application appears to be a safe and efficient method of achieving reperfusion and alleviating ischemia in the majority of patients with acute myocardial infarction. The method was not beneficial in treating unstable angina pectoris, and its potential for salvage of myocardium is yet to be assessed.

Materials and Methods

Study Group

The study group consisted of 34 patients in whom acute coronary angiography was performed between June 22, 1979 and March 30, 1980. The final diagnosis of AMI (patients 1–29) and UAP (patients 30–34) was based on serial CPK* and CK-MB values. These enzymes were normal in the UAP patients, but were increased to pathologic levels (peak CPK 879 ± 816 U/l) in the AMI patients. All patients were admitted to the hospital because they had chest pain at rest that lasted for more than 20 minutes, was not alleviated by sublingual nitroglycerin (NTG) and was presumed to be due to myocardial ischemia. The admission ECG showed changes compatible with acute myocardial ischemia in all patients except patient 34. Patient 10 was in cardiogenic shock (table 1) and patients 6, 7 and 17 were considered to be hemodynamically unstable. Patients 1, 6, 12, 22, 25 and 33 had a history of myocardial infarction.

Intracoronary streptokinase infusion was performed in all 34 patients. Acute angiography was not followed by intracoronary streptokinase infusion in one patient not included in the study group, in whom the ischemia-related coronary artery could not be identified with certainty during the study period. Acute coronary angiography was not offered to infarct patients in whom myocardial necrosis seemed to be completed at the time of hospital admission (i.e., those who were already free of pain or had completely lost

---

*CPK: Creatine Phosphokinase
the R waves in the infarct-related ECG leads). Additional criteria for rejection were age older than 75 years or severe associated diseases that would have precluded anticoagulation or subsequent bypass surgery.

Informed consent for the procedure was obtained from the patient and from an accompanying relative if possible. An i.v. infusion of NTG at a rate of 1.5–6 mg/hour was started in all patients in the emergency room shortly after admission, except in patient 10, who received i.v. dopamine, 1200 µg/min, and high doses of i.v. norepinephrine. Biplane left ventriculography (patient 10 excepted) and coronary angiography were performed within 1.5–15.5 hours (mean 5.6 ± 4 hours) after the onset of the pain episode for which the patient was admitted to the hospital. Left-heart catheterization was performed as previously described. At the beginning of the study a bolus of 10,000 U of heparin was administered intraarterially.

Acute Angiography and Intracoronary Interventions

The ischemia-related coronary artery was identified on the basis of electrocardiographic and angiographic criteria: 23 AMI patients had acute ST elevations; two AMI patients had symmetrical T-wave inversion (patients 20 and 21) and three AMI patients had downward-sloping ST depression (patients 13, 24 and 25). Coronary angiography revealed either a subtotal stenosis or occlusion of a corresponding vessel. In patient 13, in whom the ECG showed nonspecific ST-T changes, delayed clearing of contrast medium from the segment between the site of circumflex occlusion and the first proximal branch was taken as a sign of acute obstruction. In the UAP group, patient 33 had ST elevation in the inferior leads and severe narrowing of the right coronary artery, and patients 30–32 had symmetrical T-wave inversion in the left precordial chest leads and a high-degree stenosis of the left anterior descending coronary artery. In patient 34, who had a normal preangiography ECG and three-vessel disease, only the circumflex lesion was subtotal.

Identification of the ischemia-related coronary artery was followed by premedication for intracoronary drug therapy: aspirin (1 g i.v.) was injected to prevent formation of platelet thrombi and corticosteroids (prednisolone 0.747 mg i.v. in most patients) were applied to avoid allergic reactions to streptokinase. The catheter that had been used for coronary angiography was carefully placed in a stable position in the ostium of the right or left main coronary artery. Direct contact of the catheter with the site of obstruction or subselective catheterization of the ischemia-related vessel was avoided. A bolus of NTG (0.1–0.45 mg) was injected into the coronary artery, followed by repeat injections of contrast medium after 30 seconds and 3 minutes. Subsequently, patients 21–29 received 10 mg of sublingual nifedipine, and the coronary artery was opacified 5 minutes later. Streptokinase (Deutsche KABI GmbH; 250,000 U dissolved in 1 ml of normal saline solution) was infused into the ischemia-related main vessel at a rate of 2000 U/min through the coronary catheter. In patient 1, the rate of streptokinase infusion was 1000 U/min. In patients 1–17, streptokinase infusion was preceded by intracoronary injection of a bolus of streptokinase (10,000–20,000 U dissolved in 5 ml of normal saline). The soft tip of a 0.032-inch, movable-core guide wire was passed beyond the obstruction before streptokinase infusion in patient 2 and after 78 minutes of streptokinase infusion in patient 25. Streptokinase infusion was interrupted for repeat injection of contrast medium every 15 minutes or whenever there was a change of symptoms or ECG. (Leads I, II, III were monitored continuously throughout the study.) Arterial blood pressure was determined every 5 minutes.

The streptokinase infusion was terminated after 60 minutes in the majority of patients to avoid major alterations of coagulation factors. In patients 17–19, 23, 25 and 28 the duration of enzyme infusion was extended up to 95 minutes because the angiographic result did not seem satisfactory after 60 minutes or because the patient still complained of chest pain. In patients 2–4, 9, 16 and 20, the infusion was terminated earlier because reperfusion had been achieved and chest pain had subsided. The total dose of streptokinase was 128,000 ± 36,000 U.

Follow-up Treatment

After completion of the streptokinase infusion, both coronary arteries were selectively visualized again and left ventriculography was repeated in 18 AMI patients.

In the coronary care unit, i.v. heparin was administered at a dose of 800–1200 U/hour for 4–7 days, followed by long-term anticoagulation with warfarin in the AMI patients in whom intracoronary lysis had been angiographically successful (with the exception of patient 5). Clotting factors were determined before and after streptokinase application, and CPK4 and CK-MB4 were determined hourly until they returned to normal.

Aortocoronary bypass surgery was performed at various intervals after the acute study in eight AMI and three UAP patients using standard techniques (table 1). Intraaortic balloon counterpulsation was begun in patient 6 immediately after the acute study. In patient 10, the attempt to place a balloon catheter via the right and left femoral arteries during intracoronary lysis was unsuccessful due to narrowing of both iliac arteries.

Angiography was repeated 15–81 days after the acute study in 22 AMI patients (patients 1, 2, 13 and 27 after bypass surgery) and in three UAP patients. At restudy, all patients were being administered isosorbide dinitrate, β blockers and warfarin.

Evaluation of Angiographic Data

The severity of coronary artery lesions was determined by the criteria suggested by Gensini. Intracoronary intervention (streptokinase infusion,
<table>
<thead>
<tr>
<th>Pt</th>
<th>Date of angiography</th>
<th>Ischemia-related coronary lysis</th>
<th>Chronic</th>
<th>Acute collaterals</th>
<th>Other vessels (%) narrowing</th>
<th>Acute EF (%)</th>
<th>After lysis</th>
<th>Chronic EF (%)</th>
<th>Acute LVEDP (mm Hg)</th>
<th>After lysis</th>
<th>Chronic LVEDP</th>
<th>ACBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/22/79</td>
<td>LAD subtotal</td>
<td>LAD subtotal, LAD graft patent</td>
<td>+</td>
<td>RCA 75</td>
<td>44</td>
<td>—</td>
<td>58</td>
<td>35</td>
<td>—</td>
<td>16</td>
<td>LAD graft</td>
</tr>
<tr>
<td>2</td>
<td>7/01/79</td>
<td>LAD 100</td>
<td>LAD 85, LAD graft patent</td>
<td>+</td>
<td>0</td>
<td>49</td>
<td>55</td>
<td>60</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>LAD graft</td>
</tr>
<tr>
<td>3</td>
<td>7/13/79</td>
<td>RCA 100</td>
<td>RCA 90, RCA graft patent</td>
<td>0</td>
<td>LAD 70, Cx 80</td>
<td>48</td>
<td>—</td>
<td>64</td>
<td>3</td>
<td>—</td>
<td>12</td>
<td>LAD graft, Cx post. lat. graft, RCA graft</td>
</tr>
<tr>
<td>4</td>
<td>8/06/79</td>
<td>Cx subtotal</td>
<td>Cx 80</td>
<td>0</td>
<td>0</td>
<td>61</td>
<td>—</td>
<td>58</td>
<td>16</td>
<td>—</td>
<td>7</td>
<td>LAD graft</td>
</tr>
<tr>
<td>5</td>
<td>8/30/79</td>
<td>LAD 100</td>
<td>No repeat angiography</td>
<td>0</td>
<td>Cx marginal 75, RCA 50</td>
<td>48</td>
<td>51</td>
<td>—</td>
<td>20</td>
<td>17</td>
<td>—</td>
<td>LAD graft</td>
</tr>
<tr>
<td>6</td>
<td>8/31/79</td>
<td>LAD 100</td>
<td>LAD 95</td>
<td>+</td>
<td>RCA 100, Cx post. lat. 60</td>
<td>17</td>
<td>—</td>
<td>31</td>
<td>30</td>
<td>—</td>
<td>30</td>
<td>LAD graft</td>
</tr>
<tr>
<td>7</td>
<td>9/29/79</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>+</td>
<td>RCA 100, Cx marginal 100</td>
<td>29</td>
<td>45</td>
<td>46</td>
<td>30</td>
<td>—</td>
<td>10</td>
<td>LAD graft</td>
</tr>
<tr>
<td>8</td>
<td>10/16/79</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>+</td>
<td>Cx 50</td>
<td>52</td>
<td>59</td>
<td>74</td>
<td>20</td>
<td>18</td>
<td>18</td>
<td>LAD graft</td>
</tr>
<tr>
<td>9</td>
<td>10/30/79</td>
<td>RDIA 95</td>
<td>No repeat angiography</td>
<td>0</td>
<td>RCA 60, Cx post. lat. 75</td>
<td>75</td>
<td>73</td>
<td>—</td>
<td>10</td>
<td>—</td>
<td>—</td>
<td>LAD graft</td>
</tr>
<tr>
<td>10</td>
<td>10/31/79</td>
<td>RCA 100, LAD 100</td>
<td>RCA 90</td>
<td>0</td>
<td>Cx 90</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>LAD graft</td>
</tr>
<tr>
<td>11</td>
<td>11/25/79</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>+</td>
<td>Cx 60, RCA 100</td>
<td>48</td>
<td>53</td>
<td>35</td>
<td>30</td>
<td>30</td>
<td>28</td>
<td>LAD graft, Cx jump graft, RDIA graft</td>
</tr>
<tr>
<td>12</td>
<td>12/05/79</td>
<td>RCA subtotal</td>
<td>RCA 80</td>
<td>+</td>
<td>LAD 60</td>
<td>32</td>
<td>44</td>
<td>47</td>
<td>30</td>
<td>20</td>
<td>15</td>
<td>LAD graft</td>
</tr>
<tr>
<td>13</td>
<td>12/04/79</td>
<td>Cx 100</td>
<td>Cx 95, Cx graft patent</td>
<td>+</td>
<td>LAD 85, RDIA 75, RCA (distal) 90</td>
<td>73</td>
<td>—</td>
<td>68</td>
<td>15</td>
<td>—</td>
<td>12</td>
<td>Cx graft, LAD graft, RCA graft</td>
</tr>
<tr>
<td>14</td>
<td>12/14/79</td>
<td>RCA subtotal</td>
<td>RCA 85</td>
<td>0</td>
<td>LAD 85</td>
<td>75</td>
<td>66</td>
<td>72</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>LAD graft</td>
</tr>
<tr>
<td>15</td>
<td>12/17/79</td>
<td>RCA 100</td>
<td>RCA 80</td>
<td>+</td>
<td>LAD 85, Cx marginal 75</td>
<td>58</td>
<td>57</td>
<td>57</td>
<td>12</td>
<td>—</td>
<td>17</td>
<td>LAD graft</td>
</tr>
<tr>
<td>16</td>
<td>12/21/79</td>
<td>RCA subtotal</td>
<td>RCA subtotal</td>
<td>+</td>
<td>Cx 100</td>
<td>55</td>
<td>—</td>
<td>60</td>
<td>18</td>
<td>—</td>
<td>10</td>
<td>LAD graft</td>
</tr>
<tr>
<td>17</td>
<td>1/06/80</td>
<td>LAD 100</td>
<td>LAD 95</td>
<td>0</td>
<td>0</td>
<td>33</td>
<td>—</td>
<td>44</td>
<td>30</td>
<td>—</td>
<td>17</td>
<td>LAD graft</td>
</tr>
<tr>
<td>18</td>
<td>1/16/80</td>
<td>Cx 100</td>
<td>Cx 95</td>
<td>0</td>
<td>0</td>
<td>51</td>
<td>61</td>
<td>60</td>
<td>15</td>
<td>10</td>
<td>20</td>
<td>LAD graft</td>
</tr>
</tbody>
</table>

**Table 1. Angiographic Findings Before and After Lysis and in the Chronic Stage of Infarction**
<table>
<thead>
<tr>
<th>Pt</th>
<th>Date of angiography</th>
<th>Ischemie-related coronary artery (%) narrowing</th>
<th>Acute collaterals</th>
<th>Other vessels (%) narrowing</th>
<th>EF</th>
<th>LVEDP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before lysis</td>
<td>After lysis</td>
<td>Chronic</td>
<td></td>
<td>Acute</td>
<td>After lysis</td>
</tr>
<tr>
<td>19</td>
<td>2/13/80</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>LAD 75</td>
<td>+</td>
<td>RCA 95</td>
</tr>
<tr>
<td>20</td>
<td>2/24/80</td>
<td>RCA subtotal</td>
<td>RCA 90</td>
<td>RCA 80</td>
<td>+</td>
<td>Cx marginal 100, LAD 75</td>
</tr>
<tr>
<td>21</td>
<td>2/25/80</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>LAD 85</td>
<td>+</td>
<td>Cx post. lat. 75</td>
</tr>
<tr>
<td>22</td>
<td>2/27/80</td>
<td>LAD 100</td>
<td>LAD subtotal</td>
<td>No repeat angiography</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>23</td>
<td>2/28/80</td>
<td>LAD 100</td>
<td>LAD 100</td>
<td>LAD 75</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>24</td>
<td>3/04/80</td>
<td>LAD 99</td>
<td>LAD 85</td>
<td>LAD 85</td>
<td>0</td>
<td>Cx 50</td>
</tr>
<tr>
<td>25</td>
<td>3/16/80</td>
<td>RCA 100</td>
<td>RCA 90</td>
<td>RCA 50</td>
<td>+</td>
<td>Cx 90, LAD 75</td>
</tr>
<tr>
<td>26</td>
<td>3/26/80</td>
<td>LAD subtotal</td>
<td>LAD subtotal</td>
<td>No repeat angiography</td>
<td>0</td>
<td>Cx 75, RCA 100</td>
</tr>
<tr>
<td>27</td>
<td>3/27/80</td>
<td>LAD 100</td>
<td>LAD 85</td>
<td>LAD 75</td>
<td>+</td>
<td>RCA 90</td>
</tr>
<tr>
<td>28</td>
<td>3/30/80</td>
<td>RCA 100</td>
<td>RCA 100</td>
<td>RCA 100</td>
<td>+</td>
<td>LAD 75, Cx 75</td>
</tr>
<tr>
<td>29</td>
<td>3/30/80</td>
<td>LAD 100</td>
<td>LAD 90</td>
<td>LAD 90</td>
<td>0</td>
<td>Cx 75</td>
</tr>
<tr>
<td>30</td>
<td>10/02/79</td>
<td>LAD 90</td>
<td>LAD 90</td>
<td>LAD 90</td>
<td>No repeat angiography</td>
<td>0</td>
</tr>
<tr>
<td>31</td>
<td>11/21/79</td>
<td>LAD subtotal</td>
<td>LAD subtotal</td>
<td>LAD graft patent</td>
<td>0</td>
<td>RDIA 75</td>
</tr>
<tr>
<td>32</td>
<td>11/21/79</td>
<td>LAD subtotal</td>
<td>LAD subtotal</td>
<td>LAD graft patent</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>33</td>
<td>11/22/79</td>
<td>RCA 95</td>
<td>RCA 95</td>
<td>LAD 75</td>
<td>No repeat angiography</td>
<td>+</td>
</tr>
<tr>
<td>34</td>
<td>12/03/79</td>
<td>Cx subtotal</td>
<td>Cx subtotal</td>
<td>Cx graft</td>
<td>0</td>
<td>LAD 60, RCA 70</td>
</tr>
</tbody>
</table>

Abbreviations: EF = ejection fraction; LVEDP = left ventricular end-diastolic pressure; ACBS = aortocoronary bypass surgery; LAD = left anterior descending coronary artery; RCA = right coronary artery; Cx = circumflex artery; RDIA = diagonal branch; collaterals = collaterals to the ischemia-related vessel; LCA = left coronary artery; post. = posterior; lat. = lateral; + = present; 0 = absent.
NTG bolus, guide-wire recanalization) or sublingual application of nifedipine was considered successful if antegrade flow beyond an initially total obstruction was shown or if there was clear-cut increase of diameter at the site of subtotal obstruction as determined by angiography. Local wall motion of the left ventricle was qualitatively assessed from biplane cineventriculograms. Volumes were determined using the area-length method of Dodge et al. Data are presented as mean ± SD. Differences between mean values were assessed by means of the paired t test.

Results

Acute Myocardial Infarction Group

Changes in Coronary Artery Morphology

The initial injection of contrast medium showed total occlusion of the ischemia-related coronary artery in 20 patients and subtotal lesions in the remaining nine patients (table 1). All AMI patients had wall motion abnormalities corresponding to the perfusion area of the ischemia-related vessel.

Intracoronary streptokinase infusion alone or in combination with other measures was successful by angiographic criteria in 22 of 29 infarct patients (AMI1 group); the acute interventions did not result in opening the infarct vessel or in an increase of diameter at the site of subtotal lesions in seven infarct patients (AMI2 group).

In five AMI1 patients, interventions preceding streptokinase infusion were successful: Intracoronary application of NTG resulted in angiographically demonstrable changes in three patients; in patients 3 and 29, the initial total obstruction of the right and left anterior descending coronary arteries, respectively, were subtotal after intracoronary injection of NTG. There was more rapid and complete distal filling of the subtotally occluded circumflex branch in patient 4. After sublingual application of nifedipine, the initially total obstruction of the left anterior descending coronary artery in patient 21 was subtotal. In patient 2 there was delayed antegrade flow to the middle third of the left anterior descending coronary artery after a guide wire had been passed through the occlusion. In these five patients there was definite additional improvement in luminal diameter at the site of previous obstruction during streptokinase infusion.

In four patients with primary subtotal lesions (patients 12, 14, 20 and 24) that did not respond to intracoronary NTG or sublingual nifedipine, the degree of narrowing decreased during intracoronary lysis. In 12 patients with initially complete obstruction of the infarct vessel in whom the interventions preceding streptokinase application were without effect, antegrade flow was established during intracoronary streptokinase infusion (patients 5, 7, 8, 10, 11, 13, 15, 17–19, 22 and 27) (figs. 1 and 2).

The injection of contrast medium that showed patency was immediately preceded by a sudden onset of premature ventricular complexes in patients 5, 7, 13, 18, 19, 27 and 29; in the remaining patients with complete occlusions, no arrhythmias and patency were noted at the time of routine repeat opacification. Reopening of the infarct vessel was seen after 15–90 minutes of intracoronary streptokinase infusion. There seemed to be a loose correlation between lysis time required to achieve reperfusion and duration of symptoms before the acute intervention (fig. 3). Subsequent injections of contrast medium showed progressive increases in luminal diameter at the site of previous obstruction, as well as improvement of antegrade flow (fig. 1). In patient 25, the obstruction of the right coronary artery appeared more convex after 78 minutes of streptokinase infusion, but antegrade flow to the distal vessel was seen only after a guide wire had been passed beyond the occlusion. This mechanical intervention was followed by streptokinase infusion for 15 minutes, and the vessel remained patent.

The final contrast injection showed 80–90% lesions in the 22 AMI1 patients in whom intracoronary lysis was successful and a filling defect, suggestive of thrombus, in one patient of this group (fig. 2B). Repeat angiography performed before hospital discharge 25 ± 11 days after the acute intervention in 19 of these patients revealed reocclusion of the infarct vessel in patient 13, no change in 13 patients and definite further improvement in luminal diameter at the site of the initial infarct lesion in patients 15, 17, 19, 25 and 27 (fig. 2).

The acute intervention was unsuccessful in seven AMI patients (AMI2 group). Patients 1, 9, 16 and 26 had subtotal lesions and patients 6, 23 and 28 had complete obstruction of the infarct vessel. Partial recanalization occurred during streptokinase infusion in two AMI2 patients with complete obstruction of the infarct vessel. In patient 23, the filling defect became more convex and was partially stained by dye; in patient 28, a 2.5-cm segment of the occluded right coronary artery was recanalized, but the infarct vessel remained obstructed distally in both patients. Repeat angiography performed 3 weeks after the acute intervention in the three AMI2 patients with complete occlusion showed patency of the infarct vessel in patients 6 and 23 and persistent obstruction in patient 28. Repeat angiography performed in the chronic stage in two AMI2 patients with subtotal lesions (patients 1 and 16) revealed no change of these lesions.

Changes in Left Ventricular Function

Left ventricular end-diastolic pressure (LVEDP) was determined before initial angiography and immediately after streptokinase infusion in 13 AMI1 patients. LVEDP decreased from 20.4 ± 8.4 mm Hg to 15.7 ± 7.3 mm Hg (p < 0.005). At repeat angiography during the chronic stage of infarction, LVEDP was 15.9 ± 7.1 mm Hg in these patients. Ejection fraction, determined in 14 AMI1 patients before and immediately after the acute interventions, increased from 50.5 ± 12% to 54.6 ± 9% (p < 0.05). In the chronic stage of infarction, ejection fraction was also significantly higher in these patients.
(56.6 ± 12.4%) than before the acute intervention ($p < 0.01$). In comparison with the value after lysis, ejection fraction in the chronic stage was not significantly changed. Statistical analysis of hemodynamic changes was not possible in AMI$_2$ patients due to the small number of cases (table 1).

**Changes in Symptoms**

Symptoms could be evaluated only in 19 AMI$_1$ patients. Two patients had received analgesic medication at the beginning of the study and one patient was in shock.

Four AMI$_1$ patients became asymptomatic before the intracoronary interventions after initiation of i.v. NTG therapy. One patient was free of pain 5 minutes after intracoronary application of NTG. Thirteen of the remaining 14 patients who still had chest pain at the beginning of the intracoronary streptokinase infusion were asymptomatic when the streptokinase infusion was terminated; the remaining patient noted marked improvement of chest pain immediately after guide-wire recanalization, although she was not completely asymptomatic at the end of the streptokinase infusion. Improvement of symptoms occurred either immediately before or within 10 minutes after angiographic demonstration of reperfusion in patients in whom the infarct vessel was completely obstructed.
Chest pain did not improve in two of the three AMI₂ patients with complete occlusion of the infarct vessel. The third patient of this subgroup received analgesic medication. The four AMI₂ patients with subtotal obstruction of the infarct vessel became asymptomatic before intracoronary intervention after initiation of i.v. NTG therapy.

**ECG Changes**

ST elevation of more than 1 mV was present in 17 AMI₁ patients before the acute study. ST elevation was unchanged in only one of these patients after completion of the streptokinase infusion and was reduced in seven patients. In eight patients, the ST-segment had returned to baseline. There were no follow-up ECGs in patient 10, who was in cardiogenic shock.

Two of the three AMI₂ patients with complete obstruction of the infarct vessel had ST elevation that was unchanged after the acute study. The four AMI₂ patients with subtotal lesions of the infarct vessel had elevated ST segments before the acute study that returned to the baseline after completion of the intervention.

Pathologic Q waves were present before the acute study in seven AMI₁ patients. The ECG obtained after intracoronary lysis showed new Q waves in one AMI₁ patient; development of Q waves in subsequent ECGs was noted in two additional AMI₁ patients. Patho-
logic Q waves did not disappear after reperfusion.

The admission ECG of one AMI2 patient with complete obstruction of the infarct vessel showed pathologic Q waves; the remaining two patients of this subgroup developed pathologic Q waves in the coronary care unit. Immediate or late development of new Q waves was not observed in the four AMI2 patients with subtotal lesions of the infarct vessel.

Complications and Hospital Course

In patient 10, who died 3 hours after reperfusion, systolic left ventricular pressure could not be raised above 60 mm Hg before intracoronary streptokinase application, despite maximal doses of vasopressors. Coronary angiography revealed occlusion of the left anterior descending and right coronary arteries and absence of collaterals. Streptokinase infusion into the right coronary artery resulted in patency within 15 minutes. Subsequently, left ventricular pressure rose transiently to 85 mm Hg. An intraaortic balloon catheter could not be passed beyond the iliac arteries due to peripheral atherosclerosis. Ventricular fibrillation occurred repeatedly before and after reperfusion. The patient died in refractory cardiogenic shock. Autopsy revealed acute anteroseptal and inferior infarction, acute occlusion of the left anterior descending coronary artery and atheromatous narrowing of the right coronary artery with an intimal tear and remnants of an acute thrombus.

Patient 5, who was not placed on full-dose, long-term anticoagulants because of arterial hypertension, suffered an anteroseptal reinfarction 34 days after the acute study and died in cardiogenic shock. Patient 11 died suddenly 10 weeks after the acute intervention and 7 days after bypass surgery. Autopsy revealed fresh thrombotic occlusion of a vein graft. All other patients were alive and well at the time of submission of this paper.

In patients 2 and 5, surgical revision of a femoral artery puncture was necessary after the acute study due to local hemorrhage. Fibrinogen had fallen from 480 mg% to 450 mg% in patient 2 and from 600 mg% to 480 mg% in patient 5. After the acute intervention in both patients, thrombin time was more than 5 minutes.

Ventricular fibrillation, which occurred in patient 3 when a transvenous pacemaker wire was advanced into the right ventricle during the acute study, could be controlled by defibrillation.

The premature ventricular complexes that immediately preceded angiographic demonstration of reperfusion in seven patients subsided spontaneously within 10 minutes in six patients. In patient 29, the premature ventricular complexes were multifocal, refractory to i.v. xylazine and persisted for 30 minutes. Three and one-half hours after reperfusion this patient had a short bout of ventricular fibrillation that stopped spontaneously. Patient 2 had ventricular fibrillation 18 hours after the acute study.

To date, aortocoronary bypass surgery has been performed within 1 day to 8 weeks after reperfusion in six AMI1 patients and is scheduled to be performed in an additional four AMI1 patients (table 1). The indications for surgery were recurrent ischemic chest pain at rest in two patients and during exercise in seven patients. The first patient (patient 2) was operated because of ventricular fibrillation in the presence of a high-degree lesion of the left anterior descending coronary artery. Intraoperative inspection revealed active contraction of the segments perfused by the infarct vessel in all six AMI1 patients. Grafts to the infarct vessel were constructed in five of these patients; in patient 14 the distal RCA was not graftable (table 1). In two AMI2 patients (patients 1 and 26), the subtotaly obstructed left anterior descending coronary artery did not respond to intracoronary NTG or lysis and had to be revascularized because of persistent pain.

Unstable Angina Pectoris Group

The most severe coronary artery lesions in the five patients with UAP were subtotal lesions. Intracoronary injection of NTG and infusion of streptokinase did not result in an angiographically demonstrable change in luminal diameter at the site of subtotal obstruction in any of these patients.

Four UAP patients became asymptomatic before the acute study, after therapy with i.v. NTG had been initiated. Patient 31, who complained of angina pectoris during the study and during intracoronary streptokinase infusion, became transiently asymptomatic afterwards, when his blood pressure was lowered by an i.v. sodium nitroprusside infusion. Subsequently, patient 33 could be kept stable on oral nitrates and $\beta$ blockers. Patient 30 developed delirium tremens and his symptoms could not be evaluated; follow-up ECGs showed repeatedly deep symmetrical T-wave inversion without enzyme rise. He finally stabilized on medical therapy. Patients 31, 32 and 34 could not be weaned from parenteral medication (NTG or nitroprusside) without developing severe ischemic pain associated with transient ST-T changes. Stabilization was achieved by aortocoronary bypass surgery in these patients.

Clotting Factors

Clotting factors were determined in all AMI patients (patient 10 excepted) and in all UAP patients (table 2). Systemic fibrinogen and plasminogen values decreased only slightly after intracoronary lysis. Fibrin monomer complexes were elevated before the study and normal after completion of lysis. Thrombin time and thromboplastin time, which were determined before administration of streptokinase but after intraarterial administration of heparin (10,000 U), were markedly prolonged immediately before and after lysis therapy and remained in a therapeutic range 12 hours later (table 2).

Discussion

The Coronary Arteries in Acute Ischemic Syndromes

In all patients who received intracoronary streptokinase therapy, identification of the ischemia-related
Factors in immediate After 12 Hours After Streptokinase Therapy

<table>
<thead>
<tr>
<th>Fibrinogen (mg%)</th>
<th>Thromboplastin time* (Quick %)</th>
<th>Thrombin time (sec)</th>
<th>PTT (sec)</th>
<th>Fibrin monomer complexes [g%]</th>
<th>Plasminogen* (mg%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before therapy</td>
<td>451.67 ± 92.51</td>
<td>49.90 ± 16.16</td>
<td>295.54 ± 17.51</td>
<td>297.05 ± 4.37</td>
<td>0.521 ± 0.272</td>
</tr>
<tr>
<td>Immediately after therapy</td>
<td>413.45 ± 81.57</td>
<td>46.19 ± 16.48</td>
<td>296.74 ± 13.51</td>
<td>289.50 ± 6.89</td>
<td>0.062 ± 0.129</td>
</tr>
<tr>
<td>12 hours after therapy</td>
<td>437.83 ± 112.78</td>
<td>75.39 ± 17.23</td>
<td>42.60 ± 20.37</td>
<td>72.13 ± 6.57</td>
<td>—</td>
</tr>
</tbody>
</table>

*n = 22.

Coronary artery appeared to be possible based on the acute electrocardiographic and angiographic findings. In patient 10, the admission ECG showed signs of an acute inferior and a remote anteroseptal infarction; the autopsy revealed acute necrosis of both the inferior and the anteroseptal wall.

Rapid recanalization of occluded vessels and improvement of lumen at the site of high-degree lesions during intracoronary streptokinase infusion imply that fresh thrombotic material was present at the site of obstruction in 21 of 29 patients. Also, there was most likely thrombotic occlusion in the AMI patients in whom antegrade flow was not established during the acute procedure; partial recanalization occurred during streptokinase administration in two of these patients, and repeat angiography performed in the chronic stage revealed patency of the infarct vessel in the third patient. Our findings are in agreement with those of most pathologists, who found fresh coronary thrombosis in the majority of patients with acute myocardial infarction. Thrombotic occlusion was usually seen at the site of high-degree atherosclerotic lesions in pathologic studies. In our patients, the narrowing that persisted after intracoronary lysis and was still present at repeat angiography in the chronic stage of infarction was most likely due to atherosclerosis.

Improved distal filling or patency of the infarct vessel after intracoronary application of NTG, which occurred in three AMI patients, may be due to an increase in caliber of the large conductive vessels, or it may be evidence of spasm, as suggested by Oliva. The possibility of spasm cannot be ruled out in the vessels that failed to respond to intracoronary NTG. In patient 21, for example, antegrade filling of the initially obstructed infarct vessel occurred after sublingual administration of nifedipine. In all four patients in whom there was possible evidence of coronary artery spasm, the subsequent infusion of streptokinase resulted in additional and more marked improvement of lumen.

Intracoronary infusion of streptokinase did not result in angiographically demonstrable changes in four AMI patients who had subtotal lesions or in all five UAP patients who also had subtotal lesions. Most likely, narrowing of the ischemia-related coronary artery was not due to fresh thrombotic material in these nine patients, and there was no evidence of coronary artery spasm.

**Alleviation of Acute Myocardial Ischemia**

In agreement with animal experiments, rapid decrease of ST-segment elevation was seen in the majority of patients after reperfusion. Decrease of ST elevation has been interpreted as indirect evidence of salvage of myocardium by some investigators, and as possible consequence of accelerated cell necrosis by others. Rapid alleviation of ischemic pain during streptokinase infusion in AMI patients could be explained by the same two mechanisms. Extension of cell necrosis seems unlikely, however, because ejection fraction was increased immediately after streptokinase infusion. Intraoperative inspection in six patients revealed the bulk of myocardium perfused by the recanalized vessels to be viable.

Persistence of chest pain throughout the acute study in the two AMI patients who had complete obstruction of the infarct vessel and did not receive opiates indicates that myocardial ischemia was not alleviated. In the four AMI patients and the five UAP patients who had subtotal lesions of the infarct vessel, chest pain was alleviated after reduction of preload and afterload by medical therapy. The ischemic episodes were probably caused by increased myocardial oxygen demand in the presence of high-degree fixed coronary artery lesions in these subgroups.

**Technical Aspects of Intracoronary Thrombolysis**

The regimen of local lysis used in this study was successful in the 22 AMI patients as judged by alleviation of symptoms and angiographic changes. Apparently, not all thrombotic material had been dissolved at the end of the acute intervention in some of these patients, as shown by the additional improvement of lumen during the chronic stage in five AMI patients. Our technique was insufficient in three AMI patients in whom only partial or delayed recanalization of the infarct vessel was achieved.

In animal experiments, Kanmatsuse et al. showed that the efficiency of intracoronary thrombolysis depends upon the amount of lytic substance infused per minute and on the distance between the thrombus and the tip of the infusion catheter. In the present study, the infusion catheter was placed in the ostium of the right or left coronary artery. Distal placement or subselective catheterization of obstructed branches was not attempted for the sake of safety, rapidity and simplicity of the procedure.

The rate of streptokinase infusion was selected on
the basis of experience with local lysis in peripheral vessels. The total dose of streptokinase infusion was limited to a maximum of 220,000 U to avoid streptokinase-induced coagulation disorders, which would interfere with possible emergency surgery. In a preliminary study, no significant change of fibrinogen or plasminogen was seen after rapid infusion of a total dose of 50,000–100,000 U of streptokinase. However, there was a significant, albeit moderate, reduction of both fibrinogen and plasminogen after 275,000 U of streptokinase. In the present study, only minor decrease of systemic fibrinogen and plasminogen levels was observed. Bleeding from the arterial puncture site in two patients was due to heparinization, which resulted in marked prolongation of thrombin time, rather than to fibrinolytic therapy.

Reperfusion might be achieved more efficiently by various modifications of the technique, e.g., increase of streptokinase dosage, subselective infusion via small special catheters, more aggressive use of mechanical devices or different thrombolytic substances. Each of these modifications could increase the risk of the intervention.

In animal experiments, sudden release of mechanical coronary artery occlusion frequently results in dangerous arrhythmias. Moschos et al. observed that serious arrhythmias were less frequent if reperfusion was achieved gradually by intracoronary lysis. In our patients, ventricular flutter or fibrillation did not occur immediately after reperfusion, although ventricular premature complexes that were not present before the acute study developed in seven patients. In one, patient 29, the premature ventricular complexes were multifocal and lasted for 30 minutes. It cannot be determined if ventricular fibrillation occurring 3½ hours later in this patient and 18 hours after the acute study in patient 2 were related to reperfusion.

Aortocoronary Bypass Surgery

After Intracoronary Thrombolysis

Reperfusion in acute myocardial infarction has been achieved by aortocoronary bypass surgery. Intracoronary interventions performed immediately after diagnostic angiography resulted in more rapid reperfusion in 22 patients of this study. Optimal follow-up management of these patients has not been defined. There is a risk of reocclusion at the site of the persisting high-degree lesion. Reocclusion was documented angiographically in one patient in our series. It has been our policy to attempt stabilization on medical therapy, including anticoagulants, and to perform elective aortocoronary bypass surgery as soon as signs of myocardial ischemia reoccur. Aortocoronary bypass surgery was performed within 7 days after reperfusion in three patients without perioperative complications; the operation has been performed or scheduled in an additional seven patients of this group in the chronic stage of myocardial infarction.

The treatment of patients in whom the intra-coronary interventions were unsuccessful followed the same guidelines. In three patients with UAP and in two AMI patients with subtotal lesions, definite stabilization could not be accomplished by medical therapy alone but was achieved by aortocoronary bypass surgery.

References

Effects of Coronary Artery Reperfusion on Myocardial Infarct Size and Survival in Conscious Dogs

KENNETH L. BAUGHMAN, M.D., PETER R. MAROKO, M.D., AND STEPHEN F. VATNER, M.D.

SUMMARY The effects of coronary artery reperfusion at 1 and 3 hours after coronary artery occlusion were examined on myocardial infarct size and survival in conscious dogs. Left circumflex coronary artery occlusion was induced by inflating an hydraulic occluder and confirmed thereafter by measuring the absence of coronary blood flow. Of the 77 dogs that underwent coronary artery occlusion, 18 died within 1 hour. Of the 59 remaining dogs, permanent coronary artery occlusion was carried out in 31 dogs, 12 underwent reperfusion after 1 hour and 16 underwent reperfusion after 3 hours. Survival at 1 week was enhanced significantly (p < 0.01) by reperfusion carried out at either 1 or 3 hours; only 29% of dogs with permanent coronary artery occlusion survived, whereas 83% and 75% of dogs survived 1 week with reperfusion at 1 hour and 3 hours, respectively. Average infarct size at 1 week was smaller in dogs with reperfusion (NS). The inability to reach statistical significance was most likely the result of two factors: (1) There was a marked variation in infarct size in dogs with permanent coronary artery occlusion — infarcts averaged 21.3 ± 7.5% and ranged from 0.7–72.6% of the left ventricle. (2) Dogs that died 1–7 days after coronary artery occlusion had significantly (p < 0.05) larger infarcts (40 ± 4% of left ventricle) than those that survived 1 week in any of the three groups. Thus, if all dogs had survived 1 week, a beneficial effect on infarct size could have been demonstrated. Nevertheless, coronary artery reperfusion at either 1 or 3 hours after coronary artery occlusion induces a striking beneficial effect on survival, which is of the utmost clinical significance.

CORONARY ARTERY REPERFUSION in the form of coronary artery bypass has become one of the most important therapeutic interventions in medical practice. This procedure is most frequently carried out in patients with chronic coronary artery disease, but is also used in patients with acute myocardial ischemia and infarction.1,2 The physiologic basis for the value of this intervention is controversial, particularly in the acute phase of myocardial infarction. The results from experimental studies in anesthetized animal models have conflicted, showing either considerable improve-
Selective intracoronary thrombolysis in acute myocardial infarction and unstable angina pectoris.

P Rentrop, H Blanke, K R Karsch, H Kaiser, H Köstering and K Leitz

doi: 10.1161/01.CIR.63.2.307
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/63/2/307.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/