Comparison of Peak Serum C-Reactive Protein and Hydroxybutyrate Dehydrogenase Levels in Patients With Acute Myocardial Infarction Treated With Alteplase and Streptokinase

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Acute myocardial infarction (AMI) is associated with an acute-phase inflammatory reaction measurable by determination of serum C-reactive protein.1-5 The highest serum C-reactive protein values correlate with the size of the AMI when thrombolytic treatment is not given.6 If reperfusion by thrombolytic treatment occurs in AMI, the serum C-reactive protein values are lower than would be expected according to infarct size.3-5 These low serum C-reactive protein values are associated with a favorable survival prognosis during the first 6 months after AMI.6 In this study we investigate the infarct-related acute-phase reaction after treatment with accelerated alteplase, streptokinase, or a combination of both. We also wanted to elucidate whether the Thrombolysis in Myocardial Infarction (TIMI) patency grade of the infarct-related artery7 was associated with this acute-phase reaction.

...We studied patients who had been randomized to undergo early (90 minute) coronary angiography in the Global Utilization of Streptokinase and TPA (alteplase) for Occluded Coronary Arteries (GUSTO-I) enzyme substudy.8 Overall, 174 patients from the 553 patients in the enzyme substudy had been randomly assigned to angiography at the centers that also participated in the GUSTO-I angiographic substudy.9 Because the GUSTO-I main trial10 was unable to show any survival difference between the 2 streptokinase monotherapies, we chose to combine these groups. Accordingly, in this study we compared 3 treatment groups: (1) the accelerated alteplase group, (2) the streptokinase groups, and (3) the combination treatment group.

Blood samples were available from 146 patients, 48 of whom had been treated with alteplase, 66 with streptokinase, and 32 with the combination of streptokinase and alteplase. Blood samples for the study were drawn at the start of thrombolytic treatment and 1, 3, 5, 12, 18, 24, 36, 48, 72, and 96 hours later. They were analyzed for C-reactive protein and hydroxybu-

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**TABLE I Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Alteplase (n = 48)</th>
<th>Streptokinase (n = 63)</th>
<th>Combined Alteplase-Streptokinase (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr ± SD)</td>
<td>69 ± 12</td>
<td>61 ± 12</td>
<td>60 ± 11</td>
</tr>
<tr>
<td>Time from chest pain onset to start of thrombolysis (hours ± SD)</td>
<td>3.5 ± 1.9</td>
<td>3.5 ± 2.2</td>
<td>3.5 ± 4.7</td>
</tr>
<tr>
<td>Infarct location (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>24 (50%)</td>
<td>23 (37%)</td>
<td>21 (66%)</td>
</tr>
<tr>
<td>Inferior</td>
<td>22 (46%)</td>
<td>35 (55%)</td>
<td>10 (31%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (4%)</td>
<td>3 (8%)</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

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FIGURE 1. Serum C-reactive protein concentration after myocardial infarction in different treatment groups. A, serum C-reactive protein as a function of time after the infarction (means and 95% confidence intervals for the means). B, highest serum C-reactive protein concentrations (means and 95% confidence intervals for the means). The existence of significant differences between the groups was discovered by the analysis of variance method; significant differences were restudied by Student's t test to obtain the exact p values.

FIGURE 2. Highest serum C-reactive protein concentrations in patients with TIMI grade 0 to 2 and TIMI grade 3 blood flow in the infarct-related coronary artery (means and 95% confidence intervals of the means). The statistical significance was calculated by Student's t test. Open bar, TIMI 0 to 2 flow in the infarct-related coronary artery. Lined bar, TIMI 3 flow in the infarct-related coronary artery.

The peak C-reactive protein values were lower in patients who had TIMI grade 3 perfusion in the infarct-related coronary artery than in those with TIMI grade 0 to 2 flow (Figure 2). When the patients who had TIMI grade 0 to 2 flow were further divided into grade 2 versus grade 0 to 1 flow, the peak C-reactive protein values did not differ between these groups (82 ± 67 and 75 ± 58 mg/L). According to multivariate analysis, the peak C-reactive protein values of the patients who had TIMI grade 3 flow differed significantly (p = 0.020) from those of patients who had TIMI grade 2 flow, whereas the difference between patients who had grade 2 flow versus grade 0 to 1 flow did not quite reach statistical significance (p = 0.074). Patients who had TIMI grade 3 flow had smaller enzyme release than those who had grade 0 to 2 flow (4.0 ± 3.2 and 3.6 ± 3.7 g-Eq/L hydroxybutyrate dehydrogenase released; p = 0.008).

Among patients who died during hospitalization for whom a reliable peak serum C-reactive protein concentration could be determined, values were higher among those who survived (143 ± 122 vs 70 ± 54 mg/L; p <0.01). There were only 8 deaths in the study, however, and in only 3 of these patients was a reliable peak value of serum C-reactive protein available.

This study shows that treatment of AMI with accelerated dosing of alteplase leads to a smaller acute-phase reaction than does streptokinase treatment alone or combination treatment with streptokinase and alteplase. In the GUSTO-I enzyme substudy, Baardman et al8 showed that treatment with alteplase led to smaller infarcts, as determined from the release of hydroxybutyrate dehydrogenase, than did treatment with streptokinase. In the present subset of their patients, there was only a trend toward smaller infarcts in the alteplase-treated patients compared with other patients. A smaller sample size probably explains why we could not detect a significant difference. This finding is further supported by our finding that, in accordance with the main study, there was a significant association between infarct size and the TIMI flow grade in the infarct-related artery. However, our earlier studies3-5 have shown that in patients who undergo thrombolysis for myocardial infarction, the patency of the infarct-related artery affects the serum C-reactive protein values independent of its effect on infarct size. In this study, the lower peak C-reactive protein values
were significantly associated with complete reperfusion (TIMI grade 3 flow) in the infarct-related coronary artery. It thus seems that the better early patency of the infarct-related artery obtained with alteplase compared with streptokinase or the combination treatment\textsuperscript{13} reduces the associated acute-phase reaction.

It has been shown that the patients with TIMI grade 3 flow in the infarct-related artery have a favorable survival prognosis.\textsuperscript{13,14} We have shown that patients who undergo thrombolysis for AMI and whose serum C-reactive protein values remain low have a decreased risk of death than those whose values increase over time.\textsuperscript{6} We did not specifically examine the relation of the peak serum C-reactive protein value and early mortality in this study; nevertheless, patients who died during hospitalization and in whom the peak serum C-reactive protein value could be reliably determined had higher values than those who survived.

In conclusion, thrombolytic treatment of AMI with accelerated alteplase is associated with lower peak serum C-reactive protein values than treatment with either streptokinase or a combination of streptokinase and alteplase. The low-peak serum C-reactive protein values were associated with complete reperfusion of the infarct-related coronary artery. Thus, the more efficient reperfusion with alteplase compared with the other regimens\textsuperscript{13} may reduce the inflammatory reaction of AMI.

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Clinical and Angiographic Implications of Balloon Rupture During Coronary Stenting

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Coronary stenting is increasingly being used during percutaneous coronary interventions.\textsuperscript{1–3} This technique is currently selected not only for patients with suboptimal results or complications after balloon dilation, but also electively, in an attempt to reduce the restenosis rate.\textsuperscript{1,2} In the early days, coronary stenting was flawed by a relatively high incidence of subacute thrombosis and the requirement for prolonged anticoagulation, with its associated bleeding complications.\textsuperscript{1} Today, these 2 important limitations have been mostly overcome by improvements in stent implantation techniques.\textsuperscript{3} Intravascular ultrasound studies frequently demonstrate inadequate stent deployment (incomplete expansion, suboptimal apposition, or stent asymmetry) even in patients with excellent angiographic results, and that high inflation pressures may help to optimize the implantation of these devices.\textsuperscript{3} This new strategy, namely, using relatively high pressures in conjunction with a simple regimen of antiplatelet therapy, has been associated with ex-