An Early and Complete Reperfusion Strategy for Acute Myocardial Infarction Using Fibrinolysis and Subsequent Transluminal Therapy

— The FAST Trial —

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The efficacy and safety of fibrinolysis and subsequent transluminal (FAST) therapy were evaluated in 195 patients with acute myocardial infarction (AMI) for the early achievement of thrombolysis-in-myocardial-infarction grade 3 (TIMI-3) flow in the infarct-related artery. Intravenous thrombolysis using the optimal dose of a thrombolytic agent was initiated immediately after arrival in the emergency room, followed by coronary angiography and adjuvant percutaneous coronary intervention. A comparison of the thrombolysis alone (n=83) and thrombolysis plus intervention (n=112) groups showed significant differences in the time interval from hospital arrival to achievement of TIMI-3 flow (66.2±23.7 vs 111.6±29.6 min, p<0.0001), creatine kinase-MB release (295±201 vs 468±322 U/L, p=0.0003) and peak troponin T (23.6±16.9 vs 38.9±25.9 ng/ml, p<0.0001). No significant differences were observed in either 30-day mortality or complications. The TIMI-3 flow at the initial angiography was significantly higher with a single bolus of mutant tissue-type plasminogen activator (t-PA) monteplase than with an accelerated infusion of t-PA (60% vs 32%, p=0.005). In conclusion, the early restoration of TIMI-3 flow by FAST therapy reduced the degree of myocardial damage with a low risk of complications. TIMI-3 flow was achieved at an earlier stage with monteplase and this agent may be beneficial in the FAST therapy. (Circ J 2002; 66: 576–582)

Key Words: Acute myocardial infarction; Adjuvant percutaneous coronary intervention; Coronary reperfusion; Thrombolytic therapy

Coronary thrombolysis has been shown to be beneficial and effective for the treatment of acute myocardial infarction (AMI) in many clinical randomized megatrials and is now established as the standard reperfusion therapy. However, the patency rate of the infarct-related artery (IRA) ranges between 60% and 80% with this treatment, and reocclusion occurs in 5–15% of cases. The alternative therapy of primary percutaneous transluminal coronary angioplasty (PTCA) can achieve a recanalization rate as high as 90% but needs to be carried out within a short time frame. In 1999, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of patients with AMI stated that primary PTCA is an alternative therapy for thrombolysis if it is performed in a timely fashion (balloon inflation within 90±30min of admission) by persons skilled in the procedure and supported by experienced personnel in an appropriate laboratory environment.

The most crucial requirement for reperfusion therapy in AMI is not skill, but the earliest possible achievement of complete and sustained reperfusion. To this end, cocktail therapies using thrombolytic agents plus platelet glycoprotein IIb/IIIa inhibitors, combination therapy with glycoprotein IIb/IIIa inhibitors and primary coronary intervention, and a combination of thrombolysis and coronary intervention have been attempted.

The protocol for fibrinolysis and subsequent transluminal (FAST) therapy was prepared to establish a strategy for reperfusion therapy that complies with the 1996 ACC/AHA guidelines for the management of patients with AMI. FAST therapy aims for the earliest possible thrombolysis-in-myocardial-infarction grade 3 (TIMI-3) flow in the IRA after arrival in the emergency room.

This study evaluated the efficacy and safety of FAST therapy. The FAST I trial using the tissue-type plasminogen activators (t-PA) alteplase or tisokinase as thrombolytic agents was performed from 1997 to 1998, and the FAST II trial comparing t-PA with the mutant t-PA monteplase was performed from 1998 to 1999.

Methods

Study Subjects

The FAST trial was a prospective study conducted at 3 participating medical institutions. The study enrolled patients who presented after 30 min of continuous symptoms but within 12 h of the onset of symptoms of AMI and who had, on the basis of 12-lead electrocardiography (ECG) recording, ST-segment elevation of at least 0.1 mV in 2 or more limb leads, ST-segment elevation of at least 0.2 mV in the precordial leads, or bundle branch block. Patients were excluded from the study according to the following...
criteria: aged 75 years or older, a history of stroke or central nervous system damage, prior myocardial infarction (MI), prior coronary intervention or bypass surgery, active bleeding or bleeding diathesis, recent trauma or major surgery, and systolic blood pressure greater than 180 mmHg or diastolic blood pressure greater than 110 mmHg in the emergency room.

All patients gave written informed consent to participate in the study.

Study Methods

The FAST therapy protocol is shown in Fig 1. Patients who presented in the emergency room with ischemic-type chest discomfort were evaluated using a 12-lead ECG. Intravenous coronary thrombolysis with oral administration of aspirin (81–162 mg) was initiated immediately if the patient was considered eligible for the FAST trial. Emergency coronary angiography was performed following thrombolysis. If TIMI-3 flow was observed in the IRA, coronary angiography was discontinued and urokinase (500 U·kg⁻¹·h⁻¹) administered for 12 h. If TIMI-0, 1 or 2 flow was observed in the IRA, adjuvant coronary intervention was immediately performed. The adjuvant intervention procedure was selected according to whether frank thrombosis (ie, contrast medium was soaked into the thrombus) was present or absent. If it was evident, intracoronary flow was observed in the IRA, adjuvant coronary intervention was immediately performed. ECG, electrocardiography; ER, emergency room; FAST, fibrinolysis and subsequent transluminal coronary intervention.

The FAST I trial was carried out in accordance with the FAST therapy protocol using accelerated infusion of t-PA. The t-PA was given at the optimal dose recommended for Japanese patients (alteplase 0.75 mg/kg, half-life 6.3 min; or tisokinase 43.2 mg, half-life 4 min), with 10% of the dose administered by bolus injection and the remaining 90% by infusion over 60 min. In the FAST II trial, patients eligible for FAST therapy were alternately assigned a single bolus injection of the mutant t-PA monteplase (half-life 23.7 min) at the optimal dose for Japanese patients (27.5 kIU/kg), or an accelerated infusion of t-PA (same procedure as used for tisokinase in the FAST I trial). The percentage of patients achieving TIMI-3 flow at the time of initial angiography was compared.

Coronary angiography was evaluated by the cineangiography research group of the Nihon University School of Medicine.

Study Endpoints

Patients enrolled in the FAST I and II trials were divided into 2 groups: the intravenous thrombolysis alone group consisting of patients presenting with TIMI-3 flow at the time of initial angiography, and the thrombolysis plus adjuvant intervention group consisting of patients presenting with TIMI-0, 1 or 2 flow at the initial angiography. The 2 groups were compared according to the study endpoints.

Primary endpoints were mortality during the 30-day follow-up and the degree of myocardial damage based on the amount of creatine kinase-MB (CK-MB) released and peak cardiac troponin T levels. CK-MB and troponin T were measured in blood samples obtained every 3–12 h after arrival in the emergency room for at least 4 days. CK-MB levels were measured using an immuno-inhibition method and the amount of CK-MB released was calculated using the method developed by Norris et al. Troponin T levels were measured using an enzyme immunoassay method and the peak troponin T level was recorded. Secondary endpoints assessed were complications reported during the 30-day follow-up, including recurrent ischemia (spontaneous occurrence and in exercise-loading tests), reocclusion, reinfarction, blood transfusion, and cerebral bleeding.

Statistical Analysis

Endpoints for the continuous variables were expressed as mean±SD unless otherwise noted. The chi-square test or Fisher’s exact test was used to compare the frequency of each categorical variable. The continuous endpoints of the 2 groups were compared using an unpaired Student’s t test; all p values were 2-tailed. The percentage of patients with TIMI-3 flow at the time of initial angiography was compared between the mutant t-PA and t-PA groups in the FAST II trial using a 95% confidence interval (95% CI). A p value less than 0.05 was considered statistically significant.

Results

Patient Characteristics

From October 1997 to September 1999 (in both the FAST I and II trials), 247 AMI patients met the inclusion criteria for FAST therapy. A total of 52 patients (20.4%) were excluded from the trials on the basis of the exclusion criteria. FAST therapy was thus performed in the remaining 195 AMI patients (79.6%). The mean time intervals from arrival in the emergency room to thrombolysis and from thrombolysis to initial angiography were 21.4±19.0
and 45.2±21.9 min, respectively. At the initial angiography, 42.6% of patients (n=83) exhibited TIMI-3 flow in the IRA, 15.9% of patients (n=81) exhibited TIMI-2 flow, and 41.5% of patients (n=81) exhibited TIMI-0 or 1 flow. At the final angiography, 92.8% of patients (n=181) exhibited TIMI-3 flow in the IRA. Table 1 shows the baseline characteristics of the 83 patients in the intravenous thrombolysis alone group who achieved TIMI-3 flow at the initial angiography and of the 112 patients in the thrombolysis plus intervention group who presented with TIMI-0, 1 or 2 flow at the initial angiography and were continued on adjuvant coronary intervention. There were no significant differences between the 2 groups in terms of age, sex, time interval from the onset of AMI to arrival in the emergency room, Killip classification, frequency of pre-infarction angina, site of the IRA, multivessel disease, or coronary risk factors.

Table 1 Baseline Variables of the Treatment Groups

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis alone (n=83)</th>
<th>Thrombolysis plus intervention (n=112)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.5±8.9</td>
<td>59.2±9.0</td>
<td>0.59</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>16.9</td>
<td>15.2</td>
<td>0.75</td>
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<tr>
<td>Time from onset to emergency room (h)</td>
<td>3.2±2.8</td>
<td>3.3±2.7</td>
<td>0.80</td>
</tr>
<tr>
<td>Killip class ≥2 (%)</td>
<td>15.7</td>
<td>15.2</td>
<td>0.93</td>
</tr>
<tr>
<td>Preinfarction angina</td>
<td>59.0</td>
<td>60.7</td>
<td>0.81</td>
</tr>
<tr>
<td>Infarct related artery (%)</td>
<td>53.0/33.7/13.3</td>
<td>52.7/34.9/12.5</td>
<td>0.11</td>
</tr>
<tr>
<td>LAD/RCA/CX</td>
<td>48.2</td>
<td>49.1</td>
<td>0.90</td>
</tr>
<tr>
<td>Multivessel disease (%)</td>
<td>49.4</td>
<td>50.0</td>
<td>0.93</td>
</tr>
<tr>
<td>Risk factors (%)</td>
<td>22.9</td>
<td>24.1</td>
<td>0.84</td>
</tr>
<tr>
<td>Hypertension</td>
<td>79.5</td>
<td>80.4</td>
<td>0.88</td>
</tr>
<tr>
<td>Diabetes</td>
<td>60.2</td>
<td>59.8</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD. CX, circumflex; LAD, left anterior descending; RCA, right coronary artery.

Table 2 Time Interval From Arrival at Emergency Room to TIMI-3 Flow

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis alone (n=83)</th>
<th>Thrombolysis plus intervention (n=112)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency room arrival to thrombolysis (min)</td>
<td>21.6±18.9</td>
<td>21.2±19.1</td>
<td>0.88</td>
</tr>
<tr>
<td>Thrombolysis to initial angiography (min)</td>
<td>44.6±22.0</td>
<td>45.7±21.7</td>
<td>0.73</td>
</tr>
<tr>
<td>Emergency room arrival to TIMI-3 flow (min)</td>
<td>66.2±23.7 (n=83)</td>
<td>111.6±29.6 (n=98)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD. TIMI, Thrombolysis In Myocardial Infarction.

Table 3 Primary and Secondary Study Endpoints

<table>
<thead>
<tr>
<th></th>
<th>Thrombolysis alone (n=83)</th>
<th>Thrombolysis plus intervention (n=112)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoints</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK-MB released (U/L)</td>
<td>295±201 (n=81)</td>
<td>468±322 (n=110)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Peak troponin T level (ng/ml)</td>
<td>23.6±16.9 (n=81)</td>
<td>38.9±25.9 (n=110)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30-day mortality (%)</td>
<td>2.4</td>
<td>6.3</td>
<td>0.18</td>
</tr>
<tr>
<td>Secondary endpoints*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent ischemia (%)</td>
<td>16.9</td>
<td>11.6</td>
<td>0.29</td>
</tr>
<tr>
<td>Reocclusion (%)</td>
<td>1.2 (1/81)</td>
<td>3.0 (3/100)</td>
<td>0.39</td>
</tr>
<tr>
<td>Reinfarction (%)</td>
<td>1.2</td>
<td>1.8</td>
<td>0.61</td>
</tr>
<tr>
<td>Blood transfusion (%)</td>
<td>3.6</td>
<td>4.5</td>
<td>0.53</td>
</tr>
<tr>
<td>Intracerebral bleeding (%)</td>
<td>0</td>
<td>0.9</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*Incidence of complications during the 30-day period; †defined by clinical record of attending physician; ‡defined by follow-up angiography at 4 weeks after AMI or by emergency angiography during recurrent ischemia. CK, creatine kinase.

and 45.2±21.9 min, respectively. At the initial angiography, 42.6% of patients (n=83) exhibited TIMI-3 flow in the IRA, 15.9% of patients (n=81) exhibited TIMI-2 flow, and 41.5% of patients (n=81) exhibited TIMI-0 or 1 flow. At the final angiography, 92.8% of patients (n=181) exhibited TIMI-3 flow in the IRA. Table 1 shows the baseline characteristics of the 83 patients in the intravenous thrombolysis alone group who achieved TIMI-3 flow at the initial angiography and of the 112 patients in the thrombolysis plus intervention group who presented with TIMI-0, 1 or 2 flow at the initial angiography and were continued on adjuvant coronary intervention. There were no significant differences between the 2 groups in terms of age, sex, time interval from the onset of AMI to arrival in the emergency room, Killip classification, frequency of pre-infarction angina, site of the IRA, multivessel disease, or coronary risk factors.

There were no significant differences between the 2 groups in terms of the interval from emergency room arrival to thrombolysis or from thrombolysis to initial angiography. However, the time from arrival to achieving TIMI-3 flow was significantly less in the intravenous thrombolysis alone group than in the thrombolysis plus intervention group (66.2±23.7 min vs 111.6±29.6 min, p<0.0001), with a mean difference of 45.4±28.6 min (Table 2).

Of the 14 patients who failed to achieve TIMI-3 flow in the thrombolysis plus intervention group, 11 achieved TIMI-0 or 1 flow and 3 achieved TIMI-2 flow.

Study Outcomes

Table 3 shows the study endpoints for the 2 treatment groups. The amount of CK-MB released and the peak troponin T levels were significantly lower in the intravenous thrombolysis alone group than in the thrombolysis plus intervention group (295±201 vs 468±322 U/L, p=0.0003, and 23.6±16.9 vs 38.9±25.9 ng/ml, p<0.0001, respectively). The relative reduction in the amount of CK-MB released and peak troponin T levels was 37% and 39.3%, respectively. The 30-day mortality was lower in the intravenous thrombolysis alone group, but was not significantly differ-
Reperfusion therapy for AMI was not undertaken in 75% of the hospitals. Most AMI patients were subjected to initial triage and then transferred to the nearest coronary care hospital for further management. Moreover, 91% of AMI patients who were admitted to member hospitals of the Tokyo coronary care unit (CCU) network were triaged in their emergency room. An analysis of 327 patients with cardiogenic shock complicating AMI admitted to the CCU of the Tokyo CCU network within 6 h of onset of symptoms showed that thrombolysis plus adjuvant PTCA was superior to thrombolysis alone or primary PTCA in reduction of in-hospital mortality. The results suggested that the time interval from hospital arrival to achievement of TIMI-3 flow should be considered when choosing a reperfusion strategy.

**FAST Therapy**

In 1996, the second edition of the ACC/AHA guidelines for the management of patients with AMI proposed an emergency care system with initial recognition and management in the emergency department and subsequent administration of reperfusion therapy. The emergency treatment team and coronary artery intervention team of our institution cooperated with each other in establishing a protocol for the FAST therapy with the first trial initiated in October 1997. Exclusion criteria in the protocol included prior MI, as it was considered difficult for the emergency treatment team to detect AMI from an ECG pattern influenced by a prior MI. As of 1996, the ACC/AHA guidelines argued against the routine use of adjuvant PTCA in a prior study, adjuvant PTCA was useful in AMI patients with absent or poor collateral development at initial angiography within 12 h of the onset of AMI and contributed to preventing an increase in left ventricular end-diastolic volume in patients whose IRA was the left anterior descending artery, and to reducing the incidence of serious right ventricular infarction in patients whose IRA was the right coronary artery. Accordingly, adjuvant PTCA was indicated for absent or poor collateral development, and even with well developed collateral development if ischemia persisted.

In the FAST I trial, only 38.9% of patients treated with an accelerated infusion of t-PA had TIMI-3 flow at the initial angiography. In the FAST II trial, the percentage of patients with TIMI-3 flow recorded at the initial angiography was compared between the group treated with a single bolus injection of monteplase and the group treated with t-PA (72% vs 48%, p=0.012, 95% CI: 1.23–6.32).

**Discussion**

Reperfusion Therapy in Japan

Reperfusion therapy in Japan began in 1980 with intracoronary thrombolysis using urokinase and progressed to intracoronary thrombolysis using prourokinase or t-PA. In the 1990s, primary PTCA became the standard reperfusion strategy for AMI, giving way to primary stents in recent years. However, our reperfusion strategy of thrombolysis has been in place since 1980 to encourage thrombolysis therapy for AMI in all primary facilities in Japan and since that time, a total of 2,000 AMI patients who were admitted to our institution have been treated using thrombolysis.

Thrombolytic therapy differs between Japan and the West in the lower optimal dose of the thrombolytic agents (approx 50% of the dose for urokinase, prourokinase, and t-PA), the higher percentage of early recanalization and the lower incidence of intracerebral bleeding in Japanese patients.

A survey of all 737 hospitals in Tokyo found that reperfusion therapy for AMI patients was subjected to initial triage and then transferred to the nearest coronary care hospital for further management. Moreover, 91% of AMI patients who were admitted to member hospitals of the Tokyo coronary care unit (CCU) network were triaged in their emergency room. An analysis of 327 patients with cardiogenic shock complicating AMI admitted to the CCU of the Tokyo CCU network within 6 h of onset of symptoms showed that thrombolysis plus adjuvant PTCA was superior to thrombolysis alone or primary PTCA in reduction of in-hospital mortality. The results suggested that the time interval from hospital arrival to achievement of TIMI-3 flow should be considered when choosing a reperfusion strategy.

**Fig 2** Infarct-related artery patency at the time of initial coronary angiography in the FAST II trial, comparing a single bolus injection of monteplase vs an accelerated infusion of t-PA. p=0.005 for TIMI-3 flow, p=0.012 for TIMI-2 or 3 flow; monteplase vs t-PA. TIMI, thrombolysis in myocardial infarction; t-PA, tissue-type plasminogen activator.

Monteplase vs t-PA

Fig 2 shows a comparison between treatment outcomes with monteplase or t-PA in the FAST II trial. The percentage of patients with TIMI-3 flow at the time of initial angiography was significantly higher in the group treated with a single bolus injection of monteplase than with the group treated with an accelerated infusion of t-PA (60% vs 32%, p=0.005, 95% CI: 1.42–7.16). Similarly, the number of patients with either TIMI-2 or 3 flow was significantly higher in the group treated with monteplase than the group treated with t-PA (72% vs 48%, p=0.012, 95% CI: 1.23–6.32).
although mutant t-PA has the advantage of easy administration. However, because these studies evaluated thrombolysis alone, the data were considered to be different from those obtained in the FAST trial.

There was a concern that FAST therapy with thrombotic agents prior to arterial puncture for coronary angiography may lead to an increase in bleeding complications and influence the clinical outcome of adjuvant intervention. However, there was a low incidence of secondary endpoints in FAST therapy, which we believe reflects the administration of a fibrin-selective plasminogen activator with a short half-life, cautious arterial puncture, improved interventional instruments, and revised adjunctive anticoagulation regimens. No significant differences between the two groups in the incidences of recurrent ischemia, reocclusion and reinfarction were observed. However, the long-term risk of cardiac events may increase in patients undergoing thrombolysis alone for a severe stenotic IRA.

**Time to Treatment**

The mean time intervals from emergency room arrival to intravenous thrombolysis, intravenous thrombolysis to initial angiography, and emergency room arrival to initial angiography were 21.4±19, 45.2±21.9, and 67.6±23.4 min, respectively. These intervals were satisfactory, because they were all less than the time to primary PTCA balloon dilation (90±30 min) recommended by the ACC/AHA guidelines.

The results of the PACT trial, which used the same procedure as FAST therapy, were recently published. This trial involved 606 patients who were randomized to a half-dose bolus of t-PA or placebo followed by immediate angiography with angioplasty if needed. The interval between hospital arrival and study drug administration was 49 min, the interval between study drug administration and initial angiography was 49 min, and the interval between hospital arrival and initial angiography was 98 min. These time differences between the PACT and FAST trials arose from the handling of patients in the emergency room. The time differences to TIMI-3 flow with and without adjuvant intervention was similar in both trials (42 min PACT, 45 min FAST). In the PACT trial, early TIMI-3 flow without adjuvant or primary PTCA was effective in preserving left ventricular function. In the FAST trial, early TIMI-3 flow produced by intravenous thrombolysis alone reduced the degree of myocardial damage as shown by the amount of CK-MB released (37% relative reduction, \( p=0.0003 \)) and peak troponin T levels (39% relative reduction, \( p<0.0001 \)), compared with thrombolysis plus intervention. In the present study, the degree of myocardium damage in AMI was estimated by the amount of CK-MB released and peak troponin T. Although the amount of CK released overestimates the myocardium damage in reperfused AMI, there is a satisfactory correlation between the amount of CK released and the pathological infarct size or the left ventricular ejection fraction. The cardiac troponins T and I are encoded by different genes in cardiac muscle: slow skeletal muscle, and fast skeletal muscle. As a result, these markers are more specific than CK-MB for myocardial injury. Troponin T is present in the myocyte in high concentrations both in a cytosolic pool (6%) and a structurally bound protein pool (94%). The release of troponin T in the structurally bound protein pool depends on disintegration of the contractile apparatus during irreversible cell damage. Troponin T has been used to measure the degree of myocardial damage in previous reports. It has been shown that peak troponin T levels are a useful assessment of infarct size in patients with reperfused AMI; troponin T levels on admission were a powerful, independent risk marker in 865 patients as seen in a substudy of the GUSTO-IIa trial, and there is a satisfactory correlation between troponin T levels during the 3 days after reperfusion, myosin light chain I levels during the 3 days after reperfusion and left ventricular function at 1 month after AMI. In the FAST and PACT trials, the mortality rate was not significantly different between the treatment groups. This seemed to be related to the population size in both trials. In the GUSTO megatrial, mortality was reduced by early reperfusion. In both trials, early TIMI-3 flow at the initial angiography salvaged the ischemic myocardium, but major differences were seen in the early TIMI-3 flow rates produced by the thrombolytic agents (60% with monteplase and 32% with t-PA in the FAST-II trial, and 33% with t-PA in the PACT trial). Therefore, we think that mutant t-PA is superior to t-PA for the earliest possible achievement of TIMI-3 flow, which facilitates salvage of ischemic myocardium, in combination reperfusion therapy using thrombolysis and coronary intervention.

**Study Limitations**

First, the FAST I trial was not a randomized controlled study. Second, the number of patients that received FAST therapy was small. Third, FAST therapy is a more invasive and expensive procedure than intravenous thrombolysis alone, although the monteplase used in the FAST therapy costs about 180,000 yen per patient, which is less than the cost of primary PTCA on the basis of the National Health Insurance Drug Price in Japan.

In an attempt to further increase the percentage of patients achieving TIMI-3 flow after thrombolysis, the FAST II trial has been initiated. This is an ongoing randomized study to compare the number of patients achieving TIMI-3 flow at the initial angiography in groups treated with monteplase (as used in the FAST II trial) or mutant t-PA using pamiteplase at the optimal dose for Japanese patients (65 kIU/kg). In addition, further research is warranted to establish a noninvasive and reliable method for judging TIMI-3 flow. It is imperative to establish an emergency care system by which monteplase can be administered to patients eligible for FAST therapy, not only in the emergency room of coronary care units, but also at any primary facility. Adjuvant intervention can be added in the coronary care unit if needed. To establish whether a patient is eligible for thrombolysis, we recommend that the results of the 12-lead ECG for triage should be sent by facsimile to an expert for interpretation and further instructions to ensure prompt administration of thrombolysis for AMI.

Reperfusion-induced arrhythmia is a well-known phenomenon in experimental studies, but research has shown it cannot be used as an independent prognostic factor in patients undergoing out-of-hospital intravenous thrombolysis. The European Myocardial Infarction Project, a multicenter, randomized, double-blind study, found that patients in the out-of-hospital treatment group received intravenous thrombolysis a median of 55 min earlier than those in the in-hospital treatment group. Death from cardiac causes was significantly less common in the group treated out-of-hospital than in the group treated in-hospital, and a higher incidence of ventricular fibrillation before admission in the group treated out-of-hospital was offset by a higher inci-
dence of this complication during hospitalization in the group treated in-hospital. In the FAST trial, we did not have any cases of reperfusion-induced fatal arrhythmia. In our previous studies, emergency angiograms of the acute coronary syndrome-related artery revealed TIMI flow grade 0–1 in 84% of the patients who lapsed into ventricular fibrillation outside the hospital. In that study, we emphasized that most cases of out-of-hospital ventricular fibrillation complicating acute coronary syndrome were induced by an ischemic myocardium caused by an occluded acute coronary syndrome-related artery. In the guidelines for cardiopulmonary resuscitation and emergency cardiovascular care issued in 2000, out-of-hospital intravenous thrombolytic therapy was recommended when a physician was present or when out-of-hospital transport time was more than 60 min.

Conclusions

FAST therapy facilitated salvage of ischemic myocardium in patients treated with thrombolysis alone who had presented with TIMI-3 flow at initial angiography, but had no influence on patients treated with an adjuvant intervention who had presented with TIMI-0, 1 or 2 flow at initial angiography. The thrombolytic agent monteplase gave evidence of this complication during hospitalization in the group treated in-hospital. In the FAST trial, we did not have any cases of reperfusion-induced fatal arrhythmia. In that study, we emphasized that most cases of out-of-hospital ventricular fibrillation complicating acute coronary syndrome were induced by an ischemic myocardium caused by an occluded acute coronary syndrome-related artery. In the guidelines for cardiopulmonary resuscitation and emergency cardiovascular care issued in 2000, out-of-hospital intravenous thrombolytic therapy was recommended when a physician was present or when out-of-hospital transport time was more than 60 min.

References


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