Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study

*Eric Bonnefoy, Frédéric Lapostolle, Alain Leizorovicz, Gabriel Steg, Eugène P McFadden, Pierre Yves Dubien, Simon Cattan, Eric Boullenger, Jacques Machecourt, Jean-Michel Lacroute, Jean Cassagnes, François Dissait, Paul Touboul, on behalf of the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) study group**

Summary

Background Although both prehospital fibrinolysis and primary angioplasty provide a clinical benefit over in-hospital fibrinolysis in acute myocardial infarction, they have not been directly compared. Our aim was to find out whether primary angioplasty was better than prehospital fibrinolysis.

Methods We did a randomised multicentre trial of 840 patients (of 1200 planned) who presented within 6 h of acute myocardial infarction with ST-segment elevation, initially managed by mobile emergency-care units. We assigned patients to prehospital fibrinolysis (n=419) with accelerated alteplase or primary angioplasty (n=421), and transferred all to a centre with access to emergency angioplasty. Our primary endpoint was a composite of death, non-fatal reinfarction, and non-fatal disabling stroke at 30 days. Analyses were by intention to treat.

Findings The median delay between onset of symptoms and treatment was 130 min in the prehospital-fibrinolysis group and 190 min (time to first balloon inflation) in the primary-angioplasty group. Rescue angioplasty was done in 26% of the patients in the fibrinolysis group. The rate of the primary endpoint was 8·2% (34 patients) in the prehospital-fibrinolysis group and 6·2% (26 patients) in the primary-angioplasty group (risk difference 1·96, 95% CI −1·53 to 5·46). 16 (3·8%) patients assigned prehospital fibrinolysis and 20 (4·8%) assigned primary angioplasty died (p=0·61).

Interpretation A strategy of primary angioplasty was not better than a strategy of prehospital fibrinolysis (with transfer to an interventional facility for possible rescue angioplasty) in patients presenting with early myocardial infarction.

Lancet 2002; **360:** 825–29
See Commentary 814

*Contributors listed at the end of the paper

Coronary Care Unit (E Bonnefoy MD, E P McFadden FRCPI, Prof P Touboul MD), **and Department of Cardiovascular Radiology** (E P McFadden), **Hôpital Louis Pradel, Hospices Civils de Lyon, Lyon, France; SAMU 93, Bobigny** (F Lapostolle MD); **Clinical Pharmacology Unit, Laennec University, Lyon** (A Leizorovicz MD); **Hôpital Bichat, Paris** (Prof G Steg MD); **SAMU 69, Lyon** (P Y Dubien MD); **CHI Le Raincy, Montfermeil** (S Cattan MD); **SAMU 31, Toulouse** (E Boullenger MD); **CHU de Grenoble, Grenoble** (Prof J Machecourt MD); **SAMU 38, Grenoble** (J-M Lacroute MD); **CHU de Clermont Ferrand, Clermont Ferrand** (Prof J Cassagnes MD); **and SAMU 63, Clermont Ferrand** (F Dissait MD)

Correspondence to: Prof Paul Touboul, Hôpital Cardio-Vasculaire et Pneumologique Louis Pradel, BP Lyon-Montchat, 69394 Lyon Cedex 03, France
(e-mail: paul.touboul@chu-lyon.fr)

Introduction

The aim of reperfusion therapy in acute myocardial infarction is to reduce mortality and morbidity. This aim is best achieved when complete and sustained patency of the infarct-related coronary artery is obtained as early as possible.[1] Primary angioplasty results in higher patency and lower rates of recurrent myocardial infarction than in-hospital fibrinolysis.[2-6] A systematic review of all randomised controlled trials, comparing primary angioplasty and in-hospital fibrinolysis, showed that mortality 30 days after myocardial infarction was lower in patients treated with primary angioplasty.[7] However, primary angioplasty imposes additional treatment delays that could attenuate its clinical benefit in everyday practice.[2-6] Delay to treatment is an essential consideration for any revascularisation strategy.[8,9] Across several trials, prehospital administration of fibrinolytic therapy was associated with a gain of 33–130 min compared with in-hospital administration.[10-12] In a meta-analysis of those trials, prehospital fibrinolysis was associated with 17% lower total mortality (p=0·03) than in-hospital fibrinolysis.[10] Moreover, fibrinolysis has lately evolved in many centres from a pharmacological stand-alone therapy to a strategy that combines fibrinolysis with urgent angioplasty (rescue) when fibrinolysis is suspected to have failed.[13,14]

Our aim was to find out whether primary angioplasty was better than a strategy of prehospital fibrinolysis followed by transfer to a centre with interventional facilities for possible rescue angioplasty.

Methods

Study organisation and participants

The trial was coordinated by the Hospices Civils de Lyon, France. 27 tertiary hospitals, all in France, and their affiliated mobile emergency-care units (Service d'Aide Médicale d'Urgence [SAMU]) took part in the study. Each of the participating hospitals was required to have experience in routine primary angioplasty for myocardial infarction and to have a 24-h on-call angioplasty team available. All participating SAMU ambulance teams included a physician and carried electrocardiographic and resuscitation equipment, including a defibrillator. The SAMU staff were already routinely diagnosing myocardial infarction and administering fibrinolytic therapy before transfer to hospital. We obtained ethical approval from an institutional review board that served all participating hospitals, and patients provided written informed consent.

We recruited patients between June 30, 1997, and Sept 30, 2000. We included individuals if they presented within 6 h of onset of symptoms of myocardial infarction (characteristic pain lasting for at least 30 min, not responsive to nitrates, with electrocardiographic ST-segment elevation of at least 0·2 mV in two or more contiguous leads, or left bundle-branch block). Reasons for exclusion were: known bleeding disorders or any contraindication to fibrinolysis; severe renal or hepatic insufficiency; aortofemoral bypass or any condition that could hamper femoral-artery access; cardiogenic shock; history of coronary-artery bypass (CABG); or current oral anticoagulant treatment. Patients could also be excluded if

the duration of transfer to the hospital was expected to exceed 1 h.

Protocol

We randomly assigned eligible patients at the site of initial management (most, at home or at their workplace) to the prehospital-fibrinolysis or primary-angioplasty treatment group. The SAMU teams were in permanent radio contact with the SAMU medical dispatcher, who obtained the randomised assignment from a central, 24-h, computerised randomisation service.

All patients received an intravenous bolus of 5000 U heparin, and 250–500 mg aspirin (orally or intravenously). Patients assigned prehospital fibrinolysis recieved an intravenous bolus of 15 mg alteplase followed by an alteplase infusion of 0·75 mg per kg bodyweight (not to exceed 50 mg) over 30 min and then 0·50 mg per kg (not to exceed 35 mg) over the next 60 min, up to a maximum total dose of 100 mg. Treatment was started by the emergency physician at the site of intervention.

Patients assigned primary angioplasty were transported immediately to hospital for coronary angiography and angioplasty, if indicated. Angioplasty was done according to local standards with the intention of re-establishing blood flow in the infarct-related artery as soon as possible. The infarct-related artery was the only target except in patients whose haemodynamic status deteriorated despite restoration of the patency of that artery. The study protocol strongly advised that in patients with stenoses of the left main stem or critical three-vessel disease, CABG should be considered in place of angioplasty. In patients whose infarct-related arteries had flow of Thrombolysis in Myocardial Infarction (TIMI) grade 3 on first angiography, the decision to undertake angioplasty was left to the judgment of the operator.

After randomisation, heparin was continued for at least 48 h. Patients with stents were treated with a thienopyridine for 1 month. In addition to aspirin, the protocol recommended use of a β-blocking agent (atenolol) in all patients and of an inhibitor of angiotensin-converting enzyme (lisinopril) in those with anterior infarcts. Coronary angiography and subsequent revascularisation were allowed in the fibrinolysis group at the discretion of the responsible physicians, but systematic angiography at the end of fibrinolysis was forbidden. In hospitals that took part in the CAPTIM study, angiography was current practice after the fibrinolytic infusion in patients with residual chest pain or electrocardiographic signs of continuing ischaemia. When appropriate, rescue angioplasty was done.

Case-report forms were forwarded to the coordinating centre for data entry and generation of queries about missing or inconsistent data. Follow-up of patients at 30 days was by self-administered questionnaire, telephone interview by a physician, or follow-up visit with a physician.

Our primary endpoint was a composite of death, non-fatal reinfarction, and non-fatal disabling stroke within 30 days. Outcomes were adjudicated by a clinical events committee; the members were not aware of treatment assignment. Secondary endpoints assessed 30 days after treatment included: cardiovascular mortality, refractory recurrent ischaemia, cardiogenic shock, severe bleeding, and emergent revascularisation (angioplasty or CABG). CT or MRI scans of the brain were requested for all patients with suspected stroke. Recurrent infarction was defined as recurrent chest pain with an associated increase in creatine kinase or troponin over the previous trough value; severe bleeding was defined as any intracranial haemorrhage or any bleeding that caused haemodynamic compromise, required blood transfusion, or both; emergent revascularisation was defined as any revascularisation prompted by either persisting ischaemia at the end of fibrinolytic administration (rescue angioplasty) or by refractory recurrent ischaemia.

Statistical analysis

From previous studies,[5] the frequency of the primary endpoint was expected to be about 12·2% in the fibrinolysis group (death 6·7%, recurrent infarction 4·7%, stroke 0·8%) and 7·2% in the primary-angioplasty group (death 5·0%, recurrent infarction 2·0%, stroke 0·2%). A sample size of 1200 patients was chosen to ensure the detection of this 5% absolute difference (relative reduction 40%) between the groups with an α error of 0·5 (two-sided) and a β error of 0·15.

We compared selected baseline characteristics and clinical endpoints between treatment groups with the χ^2 test or Fisher's exact test for discrete variables, and the Wilcoxon rank-sum test for continuous variables. Risk differences and 95% CI were used to compare treatments in terms of major clinical endpoints. We used Kaplan-Meier survival curves to analyse time to primary endpoints during follow-up, and the Cox's model to adjust for treatment effect on baseline characteristics. All tests of significance were two tailed, and analysis was by intention to treat.

As indicated in the protocol, an interim analysis of safety and efficacy was undertaken by an independent data and safety monitoring board when enrolment reached 500 patients. Because enrolment was slower than expected, duration of enrolment was extended for a year. However, the steering committee had to terminate the trial in September 2000, owing to a lack of further funding.

Role of the funding sources

AstraZeneca (Paris, France) provided lisinopril and atenolol free of charge. BIOTRONIK GmbH (Berlin, Germany) provided balloons and guide wires free of charge.

Results

Of the 840 patients enrolled in the study, 419 were assigned prehospital-fibrinolysis and 421 primary-angioplasty (figure 1). The groups were balanced in terms of baseline characteristics (table 1). The diagnosis of suspected myocardial infarction made in the prehospital setting was confirmed by the hospital physician in 94·8% of patients. The median time to randomisation was almost identical in both groups. As expected, the median time from onset of symptoms to start of reperfusion therapy was shorter in the prehospital-fibrinolysis group (table 1).

Among the 419 patients assigned prehospital fibrinolysis, 400 (95·5%) received the therapy, five (1·2%)

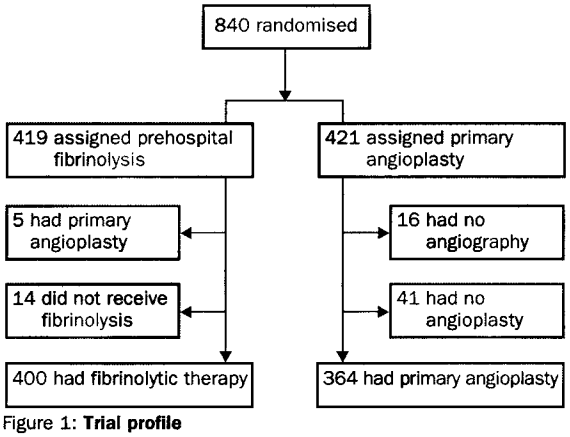

Figure 1: **Trial profile**

	Prehospital fibrinolysis (n=419)	Primary angioplasty (n=421)
Demography		
Age, years*	58 (49–69)	58 (50–68)
Age >75 years	42 (10·0%)	40 (9·5%)
Male	345 (82·5%)	343 (81·5%)
Female	74 (17·5%)	78 (18·5%)
History		
Current smokers	216 (52·6%)	205 (49·2%)
Diabetes	46 (11·1%)	57 (13·5%)
Hypertension	141 (33·9%)	146 (34·8%)
Dyslipidaemia	212 (51·1%)	215 (51·4%)
Previous CABG	0	5 (1·2%)
Previous myocardial infarction	34 (8·2%)	28 (6·7%)
Previous angioplasty	22 (5·3%)	18 (4·3%)
Characteristics at treatment		
Heart rate, beats/min*	75 (64–84)	75 (66–88)
Systolic blood pressure, mm Hg*	125 (110–140)	128 (111–140)
Anterior infarction	166 (40·2%)	178 (42·7%)
Time to randomisation, min*	107 (76–158)	108 (76–162)
Time to treatment, min*	130 (95–180)	190 (149–255)†

Percentages are calculated based on number of events/number of observations available. Data are number of patients (%) unless otherwise stated. Time shown is from onset of symptoms. *Median (IQR). †Time to first balloon inflation.

Table 1: **Baseline characteristics by treatment group**

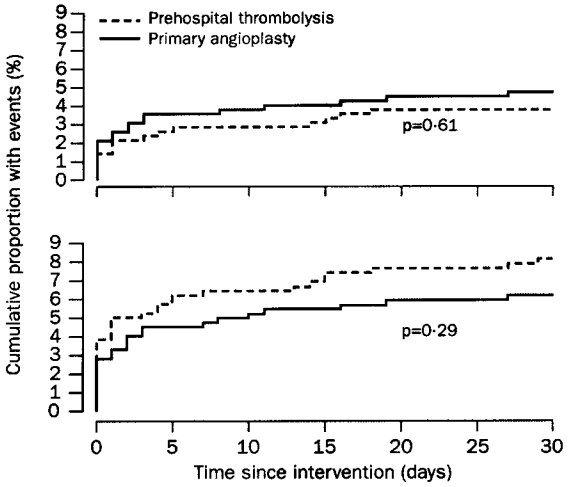

Figure 2: **Kaplan-Meier curves for deaths and cumulative rate of composite endpoint of death, reinfarction, and disabling stroke in the study patients within the 30 days after randomisation, according to treatment group**

had primary angioplasty, and 14 (3·3%) had neither treatment. Of the 421 patients assigned primary angioplasty, 405 had angiography (96·2%) and 364 had angioplasty (86·5%). Of the 57 patients (13·5%) assigned to this group who did not undergo angioplasty, 16 did not have angiography (two died; two had fibrinolysis; the indication was revised in five; and there were technical reasons in seven). 41 patients had angiography but no angioplasty (one early death; 21 open infarct-related artery with normal flow; 19 no explanation provided). The infarct-related artery was initially occluded (TIMI grade 0 or 1 flow) in 316 patients (80·4%). TIMI grade 3 flow as assessed by the operator was recorded in 333 patients after angioplasty (89·5%). No patient required bypass surgery after the procedure.

High proportions of patients in both groups received β-blockers, angiotensin-converting-enzyme inhibitors, and statins (table 2). The primary angioplasty procedure was completed by stenting in 303 patients, and intravenous glycoprotein IIb/IIIa receptor antagonists were administered in 97.

Data from the follow-up 30 days after the intervention were available for 837 patients (99·6%). Figure 2 shows

	Prehospital fibrinolysis (n=419)	Primary angioplasty (n=421)
Medication or procedure		
Angiotensin-converting-enzyme inhibitor	212 (53·8%)	194 (49·2%)
Aspirin	388 (95·8%)	395 (97·3%)
β-blocker	358 (93·0%)	334 (86·3%)
Calcium-channel blocker	35 (8·6%)	41 (10·1%)
Heparin	395 (97·4%)	391 (96·3%)
Nitrate	264 (65·2%)	227 (55·9%)
Statin	231 (57·0%)	222 (54·7%)
Ticlopidine or clopidogrel	241 (59·8%)	307 (75·6%)
Angiography up to day 30 (not scheduled by protocol)	358 (85·4%)	119 (28·3%)
Any angioplasty up to day 30 (not scheduled by protocol)	295 (70·4%)	60 (14·3%)
Urgent angioplasty	134 (33·0%)	16 (4·0%)
Persistent ischaemia (rescue)	106 (26·0%)	7 (1·7%)
Recurrent ischaemia	28 (6·7%)	9 (2·1%)
CABG surgery	6 (1·5%)	3 (0·7%)
Intra-aortic balloon pump	7 (1·7%)	14 (3·4%)

Percentages are calculated as in table 1.

Table 2: **Concomitant medications and hospital procedures**

Kaplan-Meier curves for the primary endpoint and mortality. For the primary composite endpoint, the overall event rate was 8·2% in the prehospital fibrinolysis group and 6·2% in the primary angioplasty group (p=0·29). Mortality rates did not differ significantly between the fibrinolysis and angioplasty groups (p=0·61) but there was a trend toward more stroke (p=0·12) and more recurrent infarction (p=0·13) in the prehospital fibrinolysis group (table 3).

Table 4 shows secondary endpoints. No significant differences were observed for cardiovascular death or recurrent ischaemia. The most frequent cause of death was cardiogenic shock. There was a non-significant trend toward a higher frequency of cardiogenic shock in the primary-angioplasty group (p=0·09), and cardiogenic shock between randomisation and hospital admission was observed only in that group. Severe bleeding arose in eight patients in the primary-angioplasty group and two in the prehospital-fibrinolysis group. Strokes were noted only in the prehospital fibrinolysis group, with an equal distribution of ischaemic (two) and haemorrhagic (two) causes. Overall, unplanned revascularisation (angioplasty or CABG) was done more frequently in the prehospital-fibrinolysis group than in the primary-angioplasty group (34·5% *vs* 4·7%, p<0·0001). Most of the revascularisation procedures were urgent angioplasties (33·0% in the fibrinolysis group *vs* 4·0% in the angioplasty group, p<0·0001). In the fibrinolysis group, 106 (26·0%) patients had rescue angioplasty immediately after fibrinolysis.

Discussion

Our findings indicate that primary angioplasty is no better than prehospital fibrinolysis followed by transfer for possible

	Prehospital fibrinolysis (n=419)	Primary angioplasty (n=421)	Risk difference (95% CI)	p
Endpoint				
Composite endpoint	34 (8·2%)	26 (6·2%)	1·96 (–1·53 to 5·46)	0·29
Death	16 (3·8%)	20 (4·8%)	–0·93 (–3·67 to 1·81)	0·61
Reinfarction	15 (3·7%)	7 (1·7%)	1·99 (–0·27 to 4·24)	0·13
Disabling stroke	4 (1·0%)	0	1·00 (0·02 to 1·97)	0·12

Percentages are calculated as in table 1.

Table 3: **Occurrence of primary endpoint at 30 days**

	Prehospital fibrinolysis (n=419)	Primary angioplasty (n=421)	p
Endpoint or event			
Death and recurrent ischaemia	57 (13·5%)	41 (9·8%)	0·06
Cardiovascular death	16 (3·8%)	18 (4·3%)	0·86
Recurrent ischaemia	29 (7·2%)	16 (4·0%)	0·09
Severe haemorrhage	2 (0·5%)	8 (2·0%)	0·06
Haemorrhagic stroke	2 (0·5%)	0	0·50
Ischaemic stroke	2 (0·5%)	0	0·50
Cardiogenic shock from randomisation to hospital discharge	10 (2·5%)	20 (4·9%)	0·09
Cardiogenic shock from randomisation to hospital admission	0	9 (2·1%)	0·004

Percentages are calculated as in table 1.

Table 4: **Occurrence of selected secondary endpoints and events at 30 days**

emergency coronary angioplasty in patients presenting within 6 h of an acute myocardial infarction.

Results of previous studies, comparing primary angioplasty and in-hospital fibrinolysis, suggested a definite, albeit modest, benefit of primary angioplasty over fibrinolytic therapy.[2-6] The largest of those trials, done in 1995–96, was a subset of the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) study.[5] The composite frequency of death, reinfarction, and non-fatal stroke at 30 days was significantly lower with primary angioplasty than with fibrinolysis (9·6% *vs* 13·6%, p=0·04).

The mortality rate, especially in the fibrinolysis group, was unexpectedly low in our study. There are several possible explanations. Our population could be at intermediate risk, a characteristic that would have attenuated the potential benefit of primary angioplasty.[6] Nevertheless, other fibrinolytic trials that recruited a similar population reported higher mortality.[12] The ultimate degree of flow restoration in the infarct-related coronary artery might partly account for this low mortality.[1] The prehospital-fibrinolysis group received accelerated alteplase, which is known to achieve a post-treatment TIMI 3 flow rate in 45–63% of patients.[1,15-17] However, the liberal use of rescue angioplasty in 26% of the fibrinolysis group could have resulted in a higher rate of sustained epicardial patency and thus improved the outcome.[13,14,18] Finally, the short treatment delays could have amplified the survival benefit of fibrinolysis over angioplasty. An exponential mortality reduction was noted when fibrinolytic therapy was initiated within 3 h of the onset of chest pain, and the proportional mortality reduction was much higher in patients treated within 2 h than in those treated later (44%, 95% CI 32–53, *vs* 20% 15–25, p=0·001).[19] In the CAPTIM trial, the median time to prehospital administration of fibrinolytic therapy was 50 min less than in the fibrinolysis group of the GUSTO IIb study.[5]

The lower frequency of recurrent infarction and stroke in the angioplasty group was consistent with previous findings.[2-6] In the GUSTO IIb trial, a lower reinfarction rate was an important factor in the overall benefit of angioplasty compared with fibrinolysis.[5] However, the frequency of reinfarction in our study for both treatment groups was lower than that observed in either the angioplasty or the fibrinolysis group in the GUSTO IIb trial. Subtle differences in the definition of recurrent myocardial infarction make comparisons across trials difficult. In patients who received fibrinolytic therapy, classification of such events in the early postfibrinolytic phase is difficult, and differences in the rate of rescue angioplasty or of in-hospital elective intervention might also confound comparisons. Thus, in our study, the liberal use of rescue angioplasty and of in-hospital elective intervention in the fibrinolysis group could have contributed to the low reinfarction rate.

Our findings might not be applicable to all care systems for several reasons. First, the SAMU in France has well-trained prehospital-management medical teams with an efficient centralised triage system.[20] Second, we emphasise that the CAPTIM trial compared two management strategies. The outcome in the prehospital-fibrinolysis group should be viewed as the result of a combined management strategy—early fibrinolysis, transfer to a centre with interventional facilities, and liberal use of rescue angioplasty. All hospitals in our study had on-site catheterisation laboratories and extensive experience in primary and rescue angioplasty, an important factor in outcome with these procedures.[21,22] Overall, a quarter of patients in the fibrinolysis group underwent rescue angioplasty. In this respect, transfer to a centre with on-site catheterisation facilities should not be viewed as an arbitrary choice. When patients are managed by the ambulance team and prehospital fibrinolysis has been started, they can be transferred either to the nearest hospital or to a hospital with on-site catheterisation facilities. Preliminary data from the DANAMI-2 study indicate that fibrinolysis in a hospital without on-site catheterisation facilities is associated with a higher combined rate of death, reinfarction, and stroke than is transfer for primary angioplasty.[23] The strategy developed in CAPTIM—prehospital fibrinolysis with systematic transfer to a centre with facilities for emergency angioplasty—might improve outcome in such patients.

A shortcoming of our study is that cessation of funding resulted in a lower than planned recruitment, reducing statistical power. The CI for the primary endpoint shows that there could be a real difference in the treatment effects.

Our results do not apply to excluded patients—ie, those with infarction of more than 6 h from onset of symptoms, or those with cardiogenic shock or previous CABG—for whom there is a consensus that primary angioplasty is preferable.[24] We did not exclude eldery patients but, like most studies on primary angioplasty, recruited relatively young patients. In older patients, rates of intracranial haemorrhage might be increased with alteplase.[6,25]

Data show that the potential exists for further reductions in rates of mortality and recurrent infarction after both primary angioplasty and fibrinolysis. Outcome after primary angioplasty could be improved by wider use of glycoprotein IIb/IIIa receptor antagonists.[26] The benefit of fibrinolysis might be increased by the association with low-molecular-weight heparin or glycoprotein IIb/IIIa receptor antagonists.[27] Prehospital fibrinolytic therapy has been administered in a less controlled environment than the emergency mobile unit (eg, by general practitioners[11]), a step that could greatly extend its applicability. In our study, the time required to prepare the alteplase substantially delayed fibrinolytic administration; new regimens administered as a single bolus will be particularly appropriate in this setting.[28]

Contributors

E Bonnefoy and P Touboul designed the study and took the lead in recruiting hospitals. A Leizorovicz was responsible for data management and statistical analysis. All investigators, and especially P Y Dubien, S Cattan, E Boullenger, J Machecourt, J-M Lacroute, J Cassagnes, and F Dissait, contributed to development of the protocol, planning of statistical analyses, and interpretation of findings. E Bonnefoy, F Lapostolle, A Leizorovicz, G Steg, E P McFadden, and P Touboul wrote and critically revised the report.

The CAPTIM investigators

Executive committee—P Touboul, E Bonnefoy, A Leizorovicz, J-M Lacroute, J Cassagnes, J L Blanc.

Steering committee—P Touboul (Study Chairman), A Leizorovicz (Clinical Director, Coordinating Centre), E Bonnefoy (Director, Intermediate Coordinating Centre).

Cardiology—J Beaune (Lyon); J Cassagnes (Clermont-Ferrand); S Cattan (Le Raincy); N Danchin (Vandoeuvre-les-Nancy); J L Dubois-Rande, P Dupouy (Créteil); G Grollier (Caen); K Isaaz (Saint-Etienne); T Jullien (Saint-Denis); G Kirkorian (Lyon); J Machecourt (Grenoble); J Puel (Toulouse); J C Quiret (Amiens); M Slama (Clamart); C Spaulding, PG Steg (Paris).
SAMU—J L Blanc (Saint-Etienne); F Boudet, E Boullenger (Toulouse); C Carmes (Caen); P Cristofini (Paris); F Dissait (Clermont-Ferrand); J-M Lacroute (Grenoble); F Lapostolle, P Magne (Bobigny); A Margenet (Créteil); L Nace (Nancy); B Nemitz (Amiens); J Pasteyer (Garches); G Prost (Lyon).
Writing committee—E Bonnefoy, A Leizorovicz, F Lapostolle, C Mercier, E P McFadden, G Steg, P Touboul.
Safety and efficacy monitoring committee—J P Bassand (cardiologist), B Charbonnier (cardiologist), P Goldstein (emergency physician), R Grolleau (cardiologist), Y Lambert (emergency physician).
Critical events committee—B Coppere (Lyon); L Holzapfel (Bourg-en-Bresse); D Jacques, M Lopez, N Nighoghossian (Lyon); L Ollivier (Vienne); B De Breyne (Lyon).
Mobile emergency care units (SAMU)—SAMU 93, Bogigny (F Lapostolle, C Lapandry, P Magne); SAMU 69, Lyon (G Prost, P Y Dubien, E Grand, P Petit); SAMU 75, Paris (P Cristofini); SAMU 31, Toulouse (F Boudet, W Saidi, E Boullenger, S Charpentier); SAMU 38, Grenoble (J-M Lacroute); SAMU 63, Clermont-Ferrand (F Dissait, Ch Lespiaucq); SAMU 80, Amiens (B Nemitz, C Boyer); SAMU 94, Créteil (A Margenet, C Bertrand); SAMU 92, Garches (J Pasteyer, F Templier); SAMU 14, Caen (C Carmes); SAMU 42, Saint-Etienne (J L Blanc); SAMU 54, Nancy (L Nace).
Participating hospitals (Departments of Cardiology)—Lyon (J Beaune, E Bonnefoy, G Durand De Gevigney, G Finet, M Fatemi, G Hadour, G Kirkorian); Le Raincy (S Cattan); Grenoble (J Machecourt, G Vanzetto, S Richard); Clermont-Ferrand (J Cassagnes, J R Lusson, P Motreff, D Lusson); St-Denis (T Jullien, F Drane); Amiens (J C Quiret, L Leborgne, G Jarry); Créteil (J L Dubois-Rande, S El Hamine, P Dupouy, E Teiger, F Veyssière); Toulouse, Hôpital Purpan (J Puel, M Jean, M Elbaz); Toulouse, Hôpital Rangueil (M Galinier, J Roncalli, P Cabrol); Montreuil-Sous-Bois (R Gryman, A Boccara, V Fourchard, A Kadiri); Paris, Hôpital Laribosière (P Coumel, P Beaufils, F Tarragano); Boulogne-Billancourt (J P Bourdarias, T Joseph); Paris, Hôpital Cochin (C Spaulding, P Richard, F Belaouchi); Caen (G Grollier, S Gibert); Paris, Hôpital Bichat (P G Steg, P Aubry, R Farnoud, K Picauville, E Colloc); Paris, Hôpital Tenon (A Vahanian, E Garbaz, P Michaud); Saint-Etienne (K Isaaz, A Cerisier, L Richard); Paris, Hôpital Necker (J P Metzger, F Beygui); Paris, Hôpital Boucicaut (C Guerot, K Bougrini, E Durand); Clamart (M Slama, Y Carel, P Colin); Nancy (E Aliot, G Ethevenot, R Krafft); Paris, Hôpital du Val de Grâce (J Monsegu); Vandoeuvre les Nancy (N Danchin, P Houriez); Neuilly/Seine (S Makowski, R Pilliere); Paris, Clinique Bizet (P Durand, R Cador, M Lesueur); Paris, Hôpital P Salpétrière (G Drobinski, D Thomas); Suresnes (M Francoual).
Coordinating centre—P Touboul, E Bonnefoy, A Leizorovicz, J P Teppe, C Fernandez, V Bost, A Akkal, Z Akkal, C Thien, F Bugnard, C Mercier, F Lorenzelli, N Visele, J-M Lacroute, J Cassagnes.

Conflict of interest statement

None declared.

Acknowledgments

This study was supported by a grant from the French Ministry of Health (Projet Hospitalier de Recherche Clinique, 96/045), and a research grant from AstraZeneca (Paris, France). We thank Sylvie Chabaud for statistical assistance.

References

1 The GUSTO angiographic investigators. The effects of tissue plasminogen activator, streptokinase, or both on coronary-artery patency, ventricular function and survival after acute myocardial infarction. *N Engl J Med* 1993; **329:** 1615–22.
2 Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a fibrinolytic agent followed by conservative treatment for myocardial infarction. *N Engl J Med* 1993; **328:** 685–91.
3 Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with fibrinolytic therapy for acute myocardial infarction. *N Engl J Med* 1993; **328:** 673–79.
4 Zijlstra F, de Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. *N Engl J Med* 1993; **328:** 680–84.
5 The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. *N Engl J Med* 1997; **336:** 1621–28.
6 Zahn R, Schiele R, Schneider S, et al. Primary angioplasty versus intravenous thrombolysis in acute myocardial infarction: can we define subgroups of patients benefiting most from primary angioplasty? Results from the pooled data of the Maximal Individual Therapy in Acute Myocardial Infarction Registry and the Myocardial Infarction Registry. *J Am Coll Cardiol* 2001; **37:** 1827–35.
7 Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous fibrinolytic therapy for acute myocardial infarction: a quantitative review. *J Am Coll Cardiol* 1997; **278:** 2093–98.
8 Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994; **343:** 311–22.
9 Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000; **283:** 2941–47.
10 The European Myocardial Infarction Project Group. Prehospital fibrinolytic therapy in patients with suspected acute myocardial infarction. *N Engl J Med* 1993; **329:** 383–89.
11 Rawles J. Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region Early Anistreplase Trial (GREAT). *J Am Coll Cardiol* 1994; **23:** 1–5.
12 Weaver WD, Cerqueira M, Hallstrom AP, et al. Prehospital-initiated vs hospital-initiated fibrinolytic therapy: the Myocardial Infarction Triage and Intervention Trial. *JAMA* 1993; **270:** 1211–16.
13 Ellis SG, da Silva ER, Heyndrickx G, et al. Randomised comparison of rescue angioplasty with conservative management of patients with early failure of thrombolysis for acute anterior myocardial infarction. *Circulation* 1994; **90:** 2280–84.
14 Juliard JM, Himbert D, Cristofini P, et al. A matched comparison of the combination of prehospital thrombolysis and standby rescue angioplasty with primary angioplasty. *Am J Cardiol* 1999; **83:** 305–10.
15 Cannon CP, Gibson CM, McCabe CH, et al. TNK-tissue plasminogen activator compared with front-loaded alteplase in acute myocardial infarction: results of the TIMI 10B trial. *Circulation* 1998; **98:** 2805–14.
16 den Heijer P, Vermeer F, Ambrosioni E, et al. Evaluation of a weight-adjusted single-bolus plasminogen activator in patients with myocardial infarction: a double-blind, randomised angiographic trial of lanoteplase versus alteplase. *Circulation* 1998; **98:** 2117–25.
17 Bode C, Smalling RW, Berg G, et al. Randomised comparison of coronary thrombolysis achieved with double-bolus reteplase (recombinant plasminogen activator) and front-loaded, accelerated alteplase (recombinant tissue plasminogen activator) in patients with acute myocardial infarction. *Circulation* 1996; **94:** 891–98.
18 Bar F, Vainer J, Stevenhagen J, et al. Ten-year experience with early angioplasty in 759 patients with acute myocardial infarction. *J Am Coll Cardiol* 2000; **36:** 51–58.
19 Boersma E, Maas AC, Deckers JW, Simoons ML. Early fibrinolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996; **348:** 771–75.
20 Carli P. Prehospital care in France, current status and international controversies. *Acta Anaesthesiol Scand Suppl* 1997; **110:** 69–70.
21 Every NR, Parsons LS, Hlatky M, Martin JS, Weaver WD. A comparison of fibrinolytic therapy with primary coronary angioplasty for acute myocardial infarction. *N Engl J Med* 1996; **335:** 1253–60.
22 Magid DJ, Calonge BN, Rumsfeld JS, et al. Relation between hospital primary angioplasty volume and mortality for patients with acute MI treated with primary angioplasty vs fibrinolytic therapy. *JAMA* 2000; **284:** 3131–38.
23 The DANAMI-2 study; http://www.theheart.org/index.cfm (accessed March 20, 2002).
24 Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999; **34:** 890–911.
25 Brass LM, Lichtman JH, Wang Y, Gurwitz JH, Radford MJ, Krumholz HM. Intracranial hemorrhage associated with fibrinolytic therapy for elderly patients with acute myocardial infarction: results from the Cooperative Cardiovascular Project. *Stroke* 2000; **31:** 1802–11.
26 Montalescot G, Barragan P, Wittenberg O, et al. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. *N Engl J Med* 2001; **344:** 1895–903.
27 The Assessment of the Safety and Efficacy of a New Fibrinolytic Regimen (ASSENT)-3 Investigators. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *Lancet* 2001; **358:** 605–13.
28 Assessment of the Safety and Efficacy of a New Fibrinolytic Investigators. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. *Lancet* 1999; **354:** 716–22.