Benefit of Thrombolytic Therapy Is Sustained Throughout Five Years and Is Related to TIMI Perfusion Grade 3 But Not Grade 2 Flow at Discharge

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Background Long-term follow-up in patients treated with thrombolysis for acute myocardial infarction thus far has been reported in a few studies only, and no long-term follow-up is available for patients who underwent additional percutaneous transluminal coronary angioplasty (PTCA). This report describes 5-year survival as collected in patients who received placebo, recombinant tissue plasminogen activator (rTPA), or rTPA with additional immediate PTCA in two European Cooperative Study Group trials. Determinants for long-term survival were assessed in 1043 patients discharged alive.

Methods and Results Five-year follow-up information on mortality was collected. Hospital mortality was lower after rTPA than placebo (2.5% versus 5.7%, $P=.04$) and higher after rTPA with immediate PTCA compared with rTPA without additional intervention (6.0% versus 2.2%, $P=.07$). Of the 1043 hospital survivors, data were available for 923 patients, of whom 109 died. In the placebo group, mortality after hospital discharge was 10.7% versus 11.0% in the comparative rTPA group. The patients treated with rTPA and immediate PTCA had a mortality rate of 10.5% versus 8.9% in the rTPA group without PTCA (all P=NS). Significant determinants of mortality in multivariate proportional hazards analysis were enzymatic infarct size, indicators of residual left ventricular function, number of diseased vessels and TIMI perfusion grade at discharge. Patients with TIMI grade 2 flow had mortality rates similar to those with TIMI flow grades 0 and 1, while prognosis was better in patients with TIMI flow grade 3.

Conclusions The initial in-hospital benefit of thrombolysis with intravenous rTPA is maintained throughout 5 years, with no early or late beneficial effect of systematic immediate PTCA. Enzymatic infarct size, left ventricular function, and extent of coronary artery disease are predictors for long-term survival. TIMI perfusion grade 2 at discharge should be considered as an inadequate result of therapy. (***Circulation.* 1995;92:1110-1116.**)

Key Words • thrombolysis • infarction • angioplasty

In patients with evolving myocardial infarction, thrombolytic therapy improves in-hospital survival and survival up to 1 or 2 years.[1-10] However, long-term follow-up data are scarce. The ISIS-2 study group recently reported that the improved survival in patients receiving intravenous streptokinase was sustained after 4 years,[11] while the Interuniversity Cardiology Institute from the Netherlands reported further separation of survival curves up to 8 years after treatment with intracoronary streptokinase or conventional therapy.[12] In that study, the improved long-term survival after reperfusion therapy was explained by markedly improved left ventricular function at the time of hospital discharge.[13]

To assess which factors are associated with improved long-term survival after thrombolytic therapy with recombinant tissue plasminogen activator (rTPA), 5-year follow-up data were collected in 1043 hospital survivors of two studies performed by the European Cooperative Study Group.[5,14] The following questions were addressed. Is the improved 1-year survival after thrombolytic therapy with rTPA sustained or increased at 5-year follow-up? Is there a late benefit for patients who underwent systematic immediate percutaneous transluminal coronary angioplasty (PTCA), even though such intervention did not result in any benefit at hospital discharge or at 1 or 2 years of follow-up?[9,10,14-16] Which parameters available at hospital discharge predict 5-year survival, and are these the same as those factors predicting 1-year survival?

Methods

Between May 1986 and October 1987, the European Cooperative Study Group performed two randomized prospective clinical trials in patients with acute myocardial infarction: one to investigate the effect of rTPA (alteplase) versus placebo and one to investigate the additional effect of systematic immediate PTCA to thrombolytic therapy with rTPA. Detailed protocols and initial results have been published previously.[5,14] Briefly, a total of 1088 patients with electrocardiographic evidence of myocardial infarction were enrolled provided that thrombolytic therapy could be started within 5 hours after symptom onset. Seven hundred twenty-one patients were enrolled in the double-blind rTPA/placebo trial and 367 in the rTPA/PTCA trial. Patients were given an intravenous infusion of either 100 mg alteplase or placebo (in the rTPA/placebo trial) in 3 hours. All patients received 250 mg of acetyl salicylic acid and a bolus of

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TABLE 1. Follow-up Data in the Four Treatment Groups From the rTPA/Placebo and the rTPA/PTCA Study

	Randomized	In-Hospital Death	*P*	Died Since Discharge	Alive ≥5 y	Alive, <5 y	Follow-up Actuarial Survival 5 y
Total patients	1088	45		109	814	120	
Placebo	366	21		37 (10.7)	261	47	84%
rTPA	355	9	.04	38 (11.0)	267	41	89%
rTPA	184	4	.08	16 (8.9)	145	19	86%
rTPA+PTCA	183	11	1	18 (10.5)	141	13	84%

rTPA indicates recombinant tissue plasminogen activator; PTCA, percutaneous transluminal coronary angioplasty.

Hospital mortality was significantly lower in patients treated with rTPA vs placebo in the rTPA/placebo trial ($P=.04$). Other differences were not significant. Mortality after discharge was similar in the four treatment groups. The survival difference in the rTPA/placebo trial was maintained at 5 years of follow-up (see Fig 1). Percentage of mortality in each group of patients is shown in parentheses.

5000 IU of heparin intravenously, followed by a continuous infusion of heparin 1000 IU · h^{-1}. The treatment strategies in the rTPA group of the rTPA/placebo trial and the noninvasive group of the rTPA/PTCA trial were identical. In the rTPA/PTCA trial, patients allocated to the invasive strategy underwent immediate coronary angiography and subsequently angioplasty if an occlusion or residual stenosis exceeding 60% was present. Until hospital discharge, all patients were anticoagulated with heparin, which could be replaced by coumarin after 3 days, provided that full anticoagulation was maintained. In addition, 75 to 125 mg oral acetyl salicylic acid was given every other day until hospital discharge.

Clinical data were collected and blood samples were drawn for calculation of infarct size based on α–hydroxy butyrate dehydrogenase.[17] Exercise testing, radionuclide ventriculography, coronary angiography, and left ventriculography were performed before hospital discharge. Before beginning the trial, each clinic participating in the study was assigned a specific time window for the performance of these examinations: 10 to 14, 12 to 16, 14 to 18, 16 to 20, or 18 to 22 days after allocation. β-Adrenergic blocking agents were to be prescribed unless contraindications were present. ECGs, infarct size, ventriculograms, and angiograms were centrally assessed.

There were 45 in-hospital deaths: 21, 9, 4, and 11 in the placebo, rTPA, rTPA without PTCA, and rTPA with PTCA treatment arms, respectively. Survival status was collected from all 1043 patients who were discharged alive (691 patients in the rTPA/placebo trial and 352 in the rTPA/PTCA trial). Follow-up was obtained from the treating physician, municipal registries, or the patient.

Data Analysis

Survival curves for the different treatment groups and other variables were obtained as described by Kaplan and Meier. Variables were classified in four different groups. Group 1, clinical variables, were age; sex; sum of ST elevation at the J-point on different times during hospital stay; time from symptom onset to treatment allocation; previous myocardial infarction; site of infarction; Killip class at admission; angina at rest and during effort; clinical signs of heart failure, atrial fibrillation, or pericarditis; and use of β-blockers, digitalis, diuretics, or a combination of the latter two between 24 hours and hospital discharge. A new variable was defined representing several clinical indices of impaired left ventricular function when the patient experienced one of the following: a period of systolic blood pressure below 90 mm Hg or cardiogenic shock between 24 hours and hospital discharge, New York Heart Association class III or IV at discharge, use of diuretics and/or digitalis, and not giving β-blockade to the patient. Patients in whom an exercise test was not performed on clinical grounds were also included in this variable. Group 2 variable was infarct size, as assessed from cardiac enzyme release.[17] Group 3 variables included exercise test results; systolic blood pressure rise from baseline to peak exercise; maximum heart rate during exercise; occurrence of angina; ST segment depression and elevation during exercise; and maximum workload and percentage of predicted workload achieved according to age and height. Group 4 variables included left ventricular ejection fraction from radionuclide ventriculography and variables obtained from coronary angiography and left ventriculography: TIMI perfusion grade of the infarct related vessel, extent, and severity of coronary artery disease, and end-diastolic and end-systolic volumes. In the studies, left ventricular ejection fraction was measured both by radionuclide ventriculography and by contrast angiography. The former measurement was used in the analysis because this was obtained in a larger group of patients.

For all variables mentioned above, a univariate "crude" relative risk was calculated using data from those patients of whom survival status at 5 years was known. For continuous variables, patients were categorized into three subgroups of approximately equal size or dichotomized in clinically accepted groups, as indicated in Table 3. Subsequently, mortality was assessed in each subgroup. The category with the lowest expected risk was chosen as the reference group.

To obtain independent predictors for mortality, the Cox proportional hazards model was applied, which provides a conditional probability of death for every patient at each moment during follow-up, given a certain combination of risk factors.[18] In a stepwise procedure, variables were included in the models if the probability for inclusion was less than .10. A variable was removed if the associated probability exceeded .15. Clinical data, data of the exercise test, radionuclide angiography, and angiographic data were first analyzed in clusters; those retained in the various steps were combined in the final models. The 95% confidence interval for relative risk was derived from the natural antilogarithm of the coefficient ±1.96 times the standard error.

Multivariate analysis was used to develop a composite risk score based on patient characteristics related to 5-year mortality in the univariate analysis. Relative risk estimates were obtained with Cox multivariate regression analysis. Five risk functions were designed in which clinical (subjective) parameters were compared with or combined with objective parameters obtained at hospital discharge. One model consisted of clinical data only (model I). The

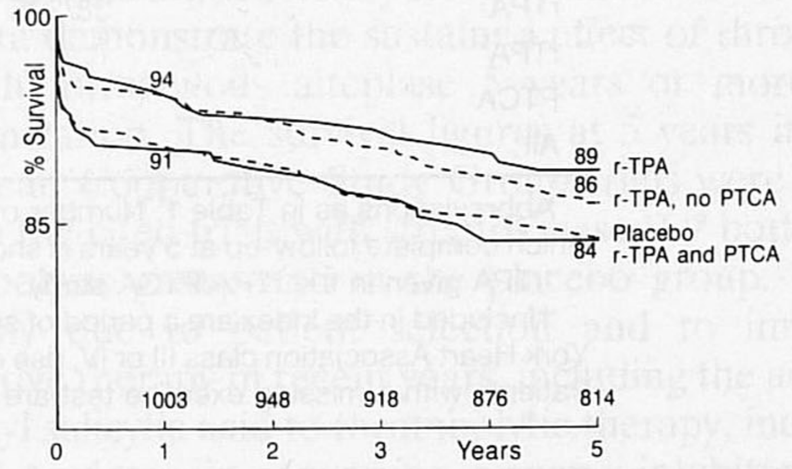

FIG 1. Survival curves after randomization of patients (n=1088) allocated to recombinant tissue plasminogen activator (rTPA) without immediate percutaneous transluminal coronary angioplasty (PTCA) or rTPA in the rTPA/placebo trial and patients allocated to conventional therapy (rTPA, no PTCA) or immediate PTCA in addition to rTPA in the rTPA/PTCA trial.

TABLE 2. Mortality Within Fifth Year After Hospital Discharge in Various Subgroups of Patients

	rTPA/Placebo Trial		rTPA/PTCA Trial			
	Placebo	rTPA	rTPA	PTCA	Overall	Risk Ratio (95% CI)
Age, y						
<60	18/184	16/170	10/122	12/101	56/577	
≥60	19/114	22/135	6/39	6/58	53/346	1.6 (1.1-2.2)
History of angina >4 wk						
No	30/251	25/242	10/122	9/114	74/729	
Yes	7/47	13/63	6/39	9/45	35/194	1.8 (1.2-2.6)
History of infarction						
No	32/274	31/284	14/150	15/147	92/855	
Yes	5/24	7/21	2/11	3/12	17/68	1.3 (1.0-1.6)
Clinical index of impaired left ventricular function†						
No	26/265	27/262	11/129	11/119	75/775	
Yes	11/33	11/43	5/32	7/40	34/148	2.3 (1.7-3.4)
ST elevation ≥2 mV at 6 h						
No	28/250	33/285	16/153	16/146	93/834	
Yes	7/33	3/6	0/3	1/6	11/48	2.0 (1.2-3.6)
Missing	2/15	2/14	0/5	1/7	5/41	1.0 (0.5-2.5)
Enzymatic infarct size, $U \cdot L^{-1}$						
<1100	13/198	22/229	10/125	11/116	56/668	
≥1100	24/97	16/76	6/36	7/43	53/252	2.5 (1.8-3.6)
Missing	0/3	. . .	. . .	. . .	0/3	. . .
Blood pressure increase during exercise, mm Hg						
≥30	14/180	17/203	12/126	12/119	55/628	
<30	19/103	16/81	3/22	3/27	41/233	2.0 (1.4-2.9)
Missing	4/15	5/21	1/13	3/13	13/62	1.9 (1.1-3.2)
Radionuclide ejection fraction, %						
≥40	18/197	19/205	11/120	5/108	53/630	
<40	17/90	18/91	5/34	11/44	51/259	2.3 (1.6-3.3)
Missing	2/11	1/9	0/7	2/7	5/34	1.8 (0.8-4.1)
No. of coronary vessels with ≥50% diameter stenosis						
<2	14/166	13/166	8/109	12/109	47/550	
≥2	22/126	23/129	8/47	4/39	57/341	2.0 (1.4-2.8)
Missing	1/6	2/10	0/5	2/11	5/32	1.8 (0.8-4.3)
TIMI flow grade at 10-22 d						
3	17/195	22/219	13/124	10/122	62/660	
2	8/32	3/26	1/10	1/3	13/71	2.0 (1.1-3.4)
1	1/14	5/16	0/5	1/3	7/38	2.0 (1.0-4.0)
0	9/50	6/33	1/12	4/20	20/115	1.9 (1.2-2.9)
Missing	2/7	2/11	1/10	2/11	7/39	1.9 (0.9-3.9)
Treatment strategy						
Placebo	37/298	. . .	. . .	. . .		. . .
rTPA	. . .	38/305	. . .	. . .		1.0 (0.7-1.5)
rTPA*	. . .	. . .	16/161	. . .		.8 (0.5-1.4)
PTCA	. . .	. . .	. . .	18/159		.9 (0.5-1.6)
All					109/923	

Abbreviations as in Table 1. Number of deaths devided by the total number of patients in each subset of which complete follow-up at 5 years is shown. Risk ratios are unadjusted and obtained by univariate analysis.

*rTPA given in the rTPA/PTCA study.

†Included in the index are a period of systolic blood pressure below 90 mm Hg or cardiogenic shock, New York Heart Association class III or IV, use of diuretics and/or digitalis, and not giving β-blockers to the patient. Patients with a missing exercise test are also included in this variable.

next model consisted of clinical data combined with enzymatic infarct size (model II), and in the third model, exercise test results were added (model III). All parameters were combined in the last model (model IV). Treatment was forced into all the models. For each model, risk estimates were calculated for each patient and compared with the observed risk.

Results

A total of 1088 patients were enrolled in the two trials, of whom 45 died in hospital. Baseline characteristics have been described in detail.[5,14] Median age was 57 years (range, 37 to 69), 80% were men, 7% had a previous

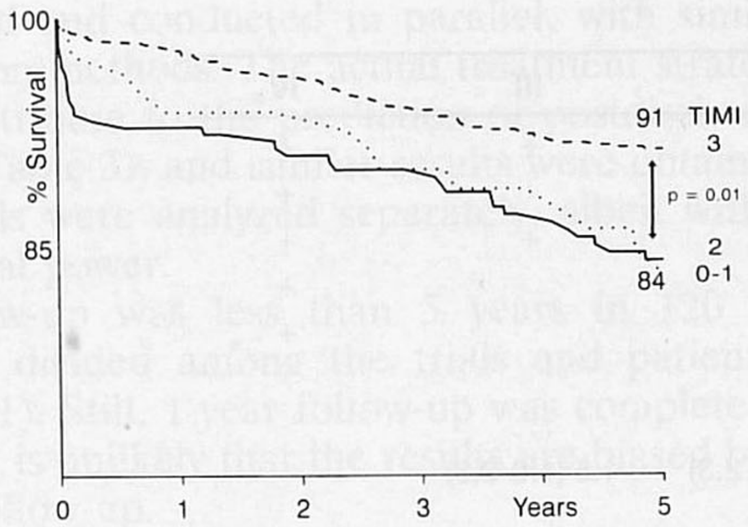

FIG 2. Survival curves after hospital discharge with stratification for different TIMI perfusion grades obtained at discharge. Patients with TIMI grades 0 and 1 are combined (solid line). The difference between patients with complete perfusion (TIMI 3; 5-year survival, 95%) and those with TIMI grades 0 to 2 (survival, 84%) was significant ($P=.01$).

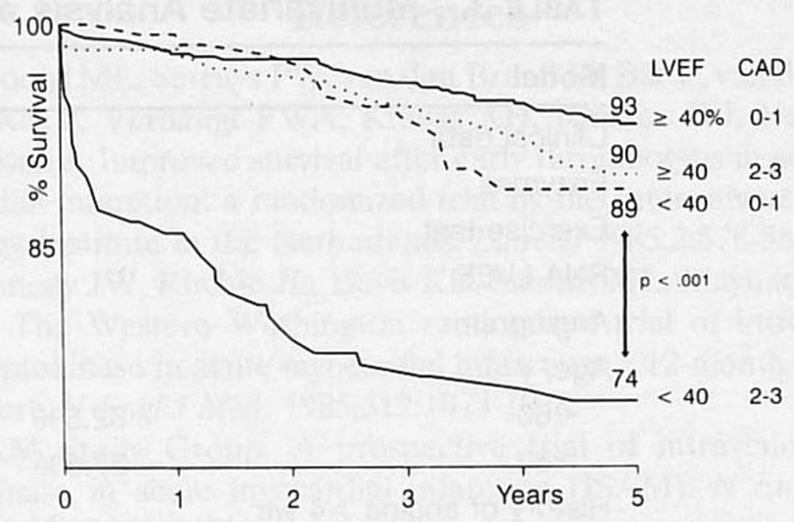

FIG 3. Survival curves after hospital discharge stratified for patients with left ventricular ejection fraction (LVEF) of 40% or greater or below 40% combined with none or one diseased vessel versus more than one diseased vessel (coronary artery disease [CAD] 0 to 1 or 2 to 3). Differences between the top three curves were not statistically significant, whereas patients discharged with impaired LVEF (<40%) and multivessel disease had worse prognoses ($P<.001$). Five-year survival rates are presented for each subgroup.

infarction, and 40% were admitted with an anterior infarction.

Complete 5-year mortality information could be obtained for 923 patients (Table 1). Median follow-up since discharge was 5.5 years, ranging from 1 day to 7.5 years. The 120 patients with incomplete follow-up (11.5%) were randomly distributed over the two studies and the four treatment groups.

Hospital mortality was 2.5% for alteplase versus 5.7% for patients receiving placebo and also 6.0% for patients allocated to additional immediate PTCA (Table 1). At 1 year and 5 years, this difference remained essentially unchanged (Fig 1). Five-year survival was similar in the two rTPA–only groups and better than either the placebo or rTPA–plus–PTCA group ($P=.06$). Five-year survival of patients discharged alive was 89%. Survival after discharge was similar in each treatment group, averaging 2.1% per year. At 5 years, as at 1 year, there was no additional beneficial effect for immediate PTCA.

Predictors for increased 5-year mortality risk after discharge angiography as obtained by univariate analysis (Table 2) were aged greater than 60 years; parameters representing residual left ventricular function: infarct size, remaining ST elevation at 6 hours, an increase of systolic blood pressure during exercise less than 30 mm Hg or inability to perform an exercise test, an ejection fraction below 40%, and the clinical index of impaired left ventricular function; as well as parameters representing the extent of coronary disease: a history of angina for more than 4 weeks, previous myocardial infarction, more than two diseased vessels, and a reduced perfusion (TIMI grade less than 3) of the infarct related artery. The relative mortality risk for incomplete perfusion (TIMI grade 2) was similar to that of TIMI grades 0 and 1, while this risk was reduced in patients with complete TIMI grade 3, flow (Fig 2). Not significant, among others, were treatment strategy, infarct location, and sex. As an example of the interaction between various parameters, Fig 3 shows survival curves for patients subdivided on ejection fraction and the extent of coronary disease.

In Table 3, we present the relative risk of each risk factor conditional on the other factors in the four risk functions as obtained by multivariate analysis. In the risk function with clinical data, only four parameters were retained (in order of decreasing importance): the clinical index of the impaired left ventricular function, history of previous infarction, ST elevation of 2 mV or more at 6 hours, and age greater than or equal to 60 years. In addition to the clinical parameters, infarct size contributed strongly to the prediction of mortality at 5 years (model II). However, systolic blood pressure rise of less than 30 mm Hg during exercise testing did not contribute independently to mortality prediction (model III).

In the final model (model IV), parameters representing left ventricular function and coronary anatomy were retained. A large infarct size and clinical findings related to an impaired ventricular function between 24 hours and discharge were associated with, respectively, 2.3- and 1.7-fold increases in mortality. Multivessel disease and TIMI perfusion grade below 3 also contributed to the risk (1.7- and 1.6-fold increases in mortality risk, respectively).

The information content of the models was compared by use of receiver operator characteristic (ROC) curves.[19] The areas under the ROC curves were almost equal in size. This implies that the predictive accuracy of the different models is similar. Thus simple clinical data suffice for long-term risk assessment after myocardial infarction.

Discussion

Sustained survival benefit of thrombolysis for acute myocardial infarction was already demonstrated for intravenous and intracoronary streptokinase.[11-13] The present data demonstrate the sustained effect of thrombolysis with intravenous alteplase 5 years or more after randomization. The survival figures at 5 years in these European Cooperative Study Group trials were higher than in the cited trials with streptokinase,[11,13] both in the thrombolysis group and in the placebo group. This is probably due to patient selection and to improved adjunctive therapy in recent years, including the addition of acetyl salicylic acid to thrombolytic therapy, increased use of angiotensin-converting enzyme inhibitors, and possibly to the high number of interventions during the first year.[9] No further separation of the survival curves occurred after discharge. This is in agreement with reports from TIMI II at 2- and 3-year follow-up[10] and with preliminary ISIS-2 follow-up results, which also

TABLE 3. Multivariate Analysis and Relative Risks

Model		I	II	III	IV
Clinical data		+	+	+	+
Enzymes			+	+	+
Exercise test				+	+
RNA LVEF					+
Angiogram					+
Age, y					
<60	62.5%	. . .	. . .	. . .	
≥60	37.5%	1.4 (1.0-2.1)	1.5 (1.0-2.3)	1.5 (1.0-2.3)	
History of angina >4 wk					
No	78.9%		. . .	. . .	
Yes	21.1%		1.6 (1.0-2.4)	1.5 (1.0-2.4)	
History of infarction					
No	93.2%	. . .	. . .	. . .	
Yes	6.8%	2.2 (1.3-3.8)	2.2 (1.3-3.8)	2.0 (1.2-3.6)	
Clinical index of impaired left ventricular function†					
No	84.0%	. . .	. . .	. . .	. . .
Yes	16.0%	2.4 (1.6-3.7)	2.0 (1.3-3.0)	1.9 (1.2-3.0)	1.7 (1.0-2.6)
ST elevation ≥2 mV at 6 h					
No	90.2%	. . .			
Yes	4.9%	2.0 (1.0-3.9)			
Missing	4.9%				
Enzymatic infarct size, $U \cdot L^{-1}$					
<1100	73.0%		. . .	. . .	. . .
≥1100	27.0%		2.5 (1.7-3.8)	2.4 (1.6-3.6)	2.3 (1.5-3.6)
No. of coronary vessels with ≥50% diameter stenosis					
<2	59.8%				. . .
≥2	36.2%				1.7 (1.1-2.5)
Missing	4.0%				0.9 (0.2-4.6)
TIMI flow grade at 10-22 d					
3	70.8%				. . .
0, 1, or 2	24.4%				1.6 (1.0-2.4)
Missing	4.9%				2.1 (0.5-8.2)
Treatment strategy					
Placebo	33.0%	. . .	. . .	. . .	. . .
rTPA	33.2%	1.0 (0.6-1.7)	1.0 (0.7-1.7)	1.1 (0.7-1.8)	1.1 (0.7-1.8)
rTPA†	17.3%	0.9 (0.5-1.6)	0.9 (0.5-1.6)	0.9 (0.5-1.8)	1.0 (0.6-2.0)
PTCA	16.5%	0.9 (0.5-1.5)	0.9 (0.5-1.6)	0.9 (0.5-1.6)	1.1 (0.7-1.8)
5-Year survival without any risk factor		0.939	0.947	0.947	0.940
Prevalence, % patients without risk factor		41.1	31.5	26.1	22.1

RNA LVEF indicates radionuclide left ventricular ejection fraction; other abbreviations as in Table 1.

Different multivariate models tested and survival for patients 5 years after hospital discharge without any risk factor. Relative risk of each risk factor was obtained by Cox multivariate regression analysis. Treatment was forced into the models; 95% confidence intervals are shown in parentheses.

†See Table 2.

show a sustained, unchanged benefit at 4 years.[11] The earlier study by the Interuniversity Institute did show further segregation of survival curves during 8-year follow-up. This can be explained by the large difference in left ventricular ejection fraction between patients with and without reperfusion therapy in that study.[13] The predictors of mortality in the present study and in the Interuniversity Institute trial were similar.

Indicators for increased mortality risk during 5 years after hospital discharge can be grouped as parameters representing infarct size or residual left ventricular function (enzymatic infarct size, the amount of ST elevation, the clinical index of impaired left ventricular function, blood pressure increase during exercise, and left ventricular ejection fraction) and parameters representing the extent of coronary disease (history of angina, previous infarction, TIMI perfusion grade, and multivessel disease). The indicators that were retained in the multivariate analysis were all interchangeable and appeared or disappeared in the model, depending on which variables were entered to represent left ventricular function or extent of coronary disease. In particular, the strongest predictor of long-term mortality risk in the final analysis, enzymatic infarct size, might be replaced by left ventricular ejection fraction without loss of accuracy in the prediction, the latter being the consequence of a large area of nonfunctioning myocardium after extensive myocardial damage.

Limitations of the Analysis

It should be appreciated that data from two studies were combined in this analysis.[5,14] These studies were

designed and conducted in parallel, with similar data collection methods. The actual treatment strategies did not contribute to the prediction of postdischarge mortality (Table 3), and similar results were obtained when the trials were analyzed separately, albeit with loss of statistical power.

Follow-up was less than 5 years in 120 patients, equally divided among the trials and patient groups (Table 1). Still, 1-year follow-up was complete in 99%. Thus, it is unlikely that the results are biased by incomplete follow-up.

In all clinical trials, actual treatment may vary, depending on the physician's preference. At 1 year, 25.5% of the patients in the noninvasive arm of the rTPA/PTCA trial had undergone PTCA or bypass surgery versus 15.6% to 18.5% in the three other groups.[9] A separate analysis was performed using actual treatment within 14 days after hospital admission. The results were very similar to the intention-to-treat analysis as presented in this report. Despite the higher intervention rate in patients allocated to rTPA in the rTPA/PTCA trial, 5-year survival was similar between the two rTPA groups (Fig 1). Thus, it is unlikely that the results have been influenced by subsequent unrecorded interventions after the first year.

Importance of Complete Coronary Perfusion for Short-term and Long-term Follow-up

It was remarkable, as demonstrated in Fig 2, that long-term prognosis for patients with incomplete perfusion, TIMI grade 2, appeared to be similar to patients with occluded (TIMI flow grades 0 or 1) vessels, while prognosis was superior in patients with complete, TIMI grade 3 flow. These observations are in concordance with other studies that reported greater myocardial salvage in patients with early complete reperfusion (TIMI grade 3) compared with those with incomplete perfusion or occlusion of the infarct related artery (TIMI grades 2, 1, or 0).[20] Immediate PTCA during thrombolytic therapy was performed in some of the patients in an attempt to improve coronary reperfusion. However, at predischarge angiography, coronary perfusion was not better after PTCA compared with patients receiving alteplase only.[14] In contrast, other studies have shown that patients undergoing direct PTCA without concomitant thrombolysis appeared to do better with a greater proportion of TIMI grade 3 flow, smaller infarct size, better preserved left ventricular function, and better survival.[21,22] This supports the notion that early, complete reperfusion is the determinant of myocardial salvage, whereas both early and late (before hospital discharge) complete perfusion are determinants of long-term survival.

Conclusions

The salutary effect of reperfusion therapy with intravenous rTPA is maintained throughout 5 years of follow-up. There was no additional late beneficial effect of systematic immediate PTCA in patients treated with rTPA. Long-term prognosis for patients with myocardial infarction could be predicted from infarct size, residual left ventricular function, and the extent of coronary artery disease at discharge. TIMI perfusion grade 2 at discharge should be considered as a result of inadequate therapy.

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