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Mortality, reinfarction, left ventricular ejection fraction and costs following reperfusion therapies for acute myocardial infarction

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The comparative efficacy of thrombolytic drugs and primary angioplasty for acute myocardial infarction have recently been studied, but long-term follow-up data have not yet been reported. We conducted a randomized trial involving 301 patients with acute myocardial infarction; 152 patients were randomized to primary angioplasty and 149 to intravenous streptokinase. Left ventricular function was assessed with a radionuclide technique both at hospital discharge and at the end of the follow-up period. Follow-up data were collected after a mean (± SD) of 31 ± 9 months. Total medical costs were calculated. At the end of the follow-up period, 5% of the angioplasty patients had died from a cardiac cause compared to 11% of the patients randomized to intravenous streptokinase, $P=0{\cdot}031$. Cardiac death or a non-fatal reinfarction occurred in 7% of angioplasty patients compared to 28% of streptokinase patients, $P<0{\cdot}001$. There was a sustained benefit of angioplasty compared to streptokinase on left ventricular function. The total medical costs in the two groups were similar. Coronary anatomy (patency and single or multivessel disease), infarct location and previous myocardial infarction were important determinants of clinical outcome and costs.

After 31 ± 9 months of follow-up, primary angioplasty compared to intravenous streptokinase results in a lower rate of cardiac death and reinfarction, a better left ventricular ejection fraction, and no increase in total medical costs. **(Eur Heart J 1996; 17: 382–387)**

Key Words: Acute myocardial infarction, streptokinase, coronary angioplasty.

Introduction

Over the past decades, the outcome of patients with acute myocardial infarction has been improved mainly by restoration of normal blood flow in the infarct-related coronary artery. Intravenous thrombolytic therapy results in an estimated reduction of early mortality between 20 and 30%[1–3]. Recently, several trials have compared primary coronary angioplasty (angioplasty without prior or concomitant administration of thrombolytic drugs) with thrombolytic therapy[4–6]. Primary angioplasty, when performed by experienced operators, restores normal (TIMI 3) blood flow in over 90% of patients[4–8]. This compares favourably with the 50–70% of patients who achieve normal flow after thrombolytic therapy[3,5,9]. However, several important questions should be resolved before primary angioplasty can be accepted as the most efficacious therapy for patients with evolving myocardial infarction. Does the superior coronary anatomy result in a more favourable clinical outcome during follow-up? Are the beneficial effects of primary coronary angioplasty on left ventricular function sustained? Is primary coronary angioplasty cost-effective? We address these issues after a follow-up of 31 months (range 15 to 50 months), in 301 patients.

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Methods

The research protocol was reviewed and approved by the institutional review board. Enrolled patients were aged less than 76 years and had symptoms of acute myocardial infarction persisting for more than 30 min accompanied by an electrocardiogram with an ST

segment elevation exceeding 1 mm (0·1 mV) in two or more contiguous leads. Patients presented within 6 h of symptom onset, or between 6 and 24 h if there was evidence of continuing ischaemia and they were without a contraindication to thrombolytic intervention[5].

Randomization and treatment

After informed consent, patients were randomly assigned to one of the two treatment modalities. All patients received aspirin and heparin. Patients randomized to streptokinase received 1·5 million units intravenously in 1 h. Patients randomized to coronary angioplasty were immediately transported to the catheterization laboratory and underwent coronary angiography. If the coronary anatomy was suitable for angioplasty, this was performed immediately using standard techniques. Coronary angiography during follow-up was used to assess sustained patency of the infarct-related artery in all patients, as previously described[7,8].

Follow-up information was obtained in October 1994 as part of the work made possible by grant 1992:321 of the Netherlands Heart Foundation. All outpatient reports were reviewed, and general practitioners as well as patients were contacted by telephone. For patients who had died during follow-up, hospital records and autopsy data were reviewed. No patient was lost to follow-up. Information was collected on mortality, the cause of death and non-fatal recurrent myocardial infarction, defined as previously described[5].

Left ventricular ejection fraction was measured with a multiple-gated equilibrium method after the in vivo labelling of red cells with 99m-Tc-pertechnetate[5] using a gamma camera (General Electric, Milwaukee, U.S.A.) with a low-energy, all purpose, parallel-hole collimator. The global ejection fraction was calculated automatically by a computer (Star View, General Electric) with the PAGE™ program. The data on ejection fractions were analysed by nuclear medicine specialists who were blinded to the clinical data.

Costs were calculated using estimates of unit costs concerning all aspects of medical care. These included hospital days (distinguishing between normal care, coronary care and postoperative intensive care), diagnostic or therapeutic procedures and medication (including the thrombolytic drugs given). Data were registered during the initial admission, during readmissions and during visits to the outpatient clinic. By general survey of patients (mostly by telephone interview) and of the referring physicians, readmissions to other hospitals could be traced and these data were added to the database. All patients were scheduled for follow-up angiography and the costs of this procedure were included in the calculations. Unit costs for procedures and hospital days were calculated on the basis of hospital administration data of 1992. These included the professional charges and were adjusted for the increased costs of procedures during the night or the weekend.

Table 1 Baseline characteristics

	Streptokinase (n=149)	Angioplasty (n=152)
Age (years)	61 ± 9	59 ± 10
Male sex	121 (81%)	127 (84%)
Anterior infarction	68 (46%)	79 (52%)
Previous infarction	21 (14%)	32 (21%)
Time onset-admission (min)	176 ± 172	195 ± 227
Killip class on admission:		
I	122 (82%)	116 (76%)
II	15 (10%)	22 (14%)
III	9 (6%)	6 (4%)
IV	3 (2%)	8 (5%)
Multivessel disease	88 (59%)	95 (63%)

Costs applied for a diagnostic catheterization were Dfl.1500, angioplasty Dfl.8000, bypass surgery Dfl.18 000, one day in the coronary care unit Dfl.1550, one day in the postoperative intensive care unit Dfl.2250, and one day on a general ward Dfl.500. Costs for streptokinase and tPA were Dfl.400 and Dfl.2000 respectively. The costs of additional pharmacological treatment were based on the average treatment costs of the various drugs according to their prices in 1992, including costs for prescription administration. Costs per month were estimated as: aspirin Dfl.10, nitrates Dfl.20, diuretics Dfl.30, coumadin Dfl.33 (including coagulation tests), anti-arrhythmic agents Dfl.35, β-blockers Dfl.60, calcium-blockers Dfl.70, angiotensin converting enzyme-inhibitors Dfl.105 and cholesterol lowering drugs Dfl.135.

Statistical analysis

All end-points were analysed according to the 'intention to treat' principle. Differences between group means were tested by two-tailed Student's t-test. A chi-square method or Fisher's exact test was used to test differences between proportions. Statistical significance was defined as a *P*-value of less than 0·05. Survival functions were calculated using the Kaplan–Meier product limit method[10]. The Mantel–Cox (or log-rank) test was applied to evaluate the differences between survival functions. Odds ratios were calculated which may be interpreted as relative risks with 95% confidence intervals[11].

Results

During the enrolment period, 149 patients were randomized to streptokinase and 152 to coronary angioplasty. Baseline characteristics were similar, as shown in Table 1. The initial results have been published[10,13]. Two patients with cardiogenic shock died immediately following randomization (one in each group). Angioplasty was performed in 140 of the 152

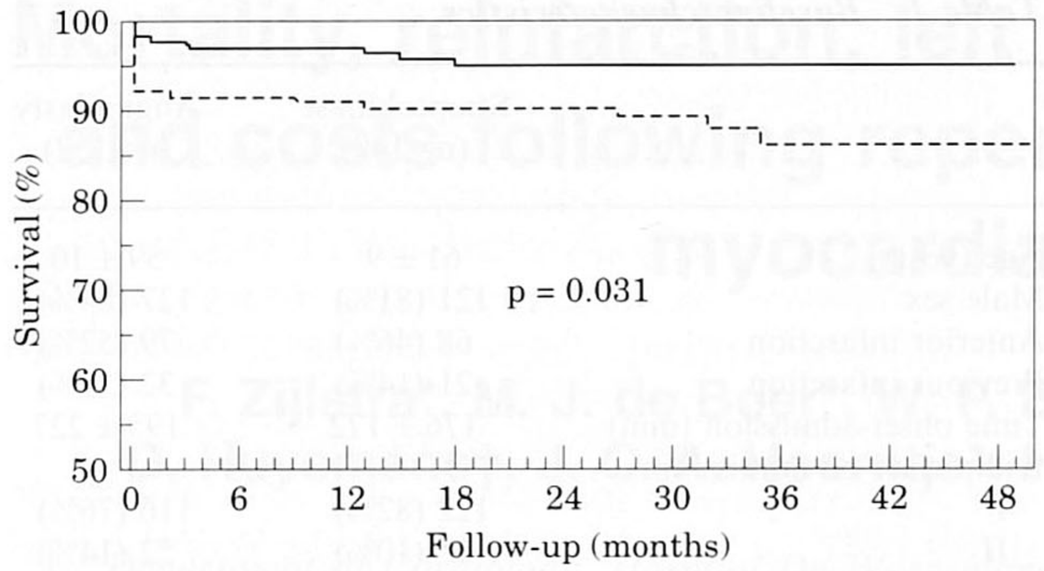

Figure 1 **Incidence of cardiac death in 301 patients with acute myocardial infarction, randomized to treatment with streptokinase (– – –) or primary angioplasty (———) ($P< 0{\cdot}031$).**

patients, and the procedure was successful in 136 (97%), with a mean time from admission to the first balloon inflation of 62 min. In four patients, angioplasty failed to reopen the infarct-related artery; three of them underwent emergency coronary artery bypass grafting. Five patients had an open infarct-related artery and were treated conservatively. Six patients with extensive coronary artery disease underwent primary coronary artery bypass grafting. All patients assigned to therapy with intravenous streptokinase were treated accordingly. The mean time from admission to start of the streptokinase infusion was 29 min. Sixteen patients with haemodynamic compromise and signs of ongoing ischaemia underwent rescue angioplasty with procedural success in 15 patients. Emergency coronary artery bypass grafting was performed in one patient.

The mean follow-up time was 31 months (SD ± 11 months). A total of 32 patients (11%) died. A non-cardiac cause of death was confirmed in eight patients; five in the angioplasty group, and three in the streptokinase group. Two patients died from strokes which were unrelated to a cardiac event during follow-up: both with CT scan confirmation of the diagnoses; five patients died of lung cancer and one from liver carcinoma. All diagnoses of malignancy were confirmed by autopsy.

Seven patients (5%) randomized to angioplasty died from a cardiac cause: cardiogenic shock or heart failure in four, and sudden death in three patients. Seventeen patients (11%) randomized to streptokinase died from a cardiac cause: stroke in one patient, cardiogenic shock or heart failure in 10 patients, and sudden death in six patients. Survival curves are shown in Fig. 1. The relative risk of cardiac death in streptokinase patients compared to angioplasty patients was 2·5 (95% confidence interval 1·1–6·1). The influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy on mortality is shown in Table 2. Patency of the infarct-related vessel, single-vessel disease and absence of a previous myocardial infarction were associated with improved long-term survival.

Reinfarctions occurred in 29 patients (19%) randomized to streptokinase compared to 5 patients (3%) randomized to angioplasty, $P=0{\cdot}001$, see Table 3. In the streptokinase group, 14 reinfarctions occurred prior to coronary angiography compared to 2 reinfarctions prior to follow-up angiography in the angioplasty

Table 2 Mortality: the influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy

	n	Discharge	Follow up
Age <65	201	3·0%	5·6%
		ns	$P=0{\cdot}04$
Age >65	100	8·0%	13·0%
Patent IRV	226	0·4%	3.1%
		$P<0{\cdot}0001$	$P<0{\cdot}0001$
Occluded IRV	75	17·3%	22·7%
SVD	117	0%	1·7%
		$P=0{\cdot}004$	$P=0{\cdot}002$
MVD	179	6·7%	11·2%
Prev. MI	53	7·5%	18·9%
		ns	$P=0{\cdot}003$
No prev. MI	248	4·0%	5·6%
Ant. MI	147	6·8%	11·6%
		ns	$P=0{\cdot}03$
Non-ant. MI	154	2·6%	4·5%
Streptokinase	149	7·4%	11·4%
		$P=0{\cdot}03$	$P=0{\cdot}03$
Angioplasty	152	2·0%	4·6%

IRV=infarct-related vessel, ant=anterior, prev=previous, MI=myocardial infarction, SVD=coronary artery disease limited to the infarct-related vessel, MVD=coronary artery disease in the IRV as well as one or both 1 other major coronary arteries.

Table 3 Reinfarction: the influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy

	n	Discharge	Follow up
Age <65	201	7·0%	10·4%
		ns	ns
Age >65	100	8·0%	13·0%
Patent IRV	226	4%	8·4%
		$P=0{\cdot}0004$	$P=0{\cdot}01$
Occluded IRV	75	17·3%	20%
SVD	117	5·1%	11·1%
		ns	ns
MVD	179	8·9%	11·7%
Prev. MI	53	13·2%	15·1%
		ns	ns
No prev. MI	248	6·0%	10·5%
Ant. MI	147	6·1%	10·9%
		ns	ns
Non-ant. MI	154	8·4%	11·7%
Streptokinase	149	13·4%	19·5%
		$P=0{\cdot}0001$	$P<0{\cdot}0001$
Angioplasty	152	1·3%	3·3%

Abbreviations as in Table 2.

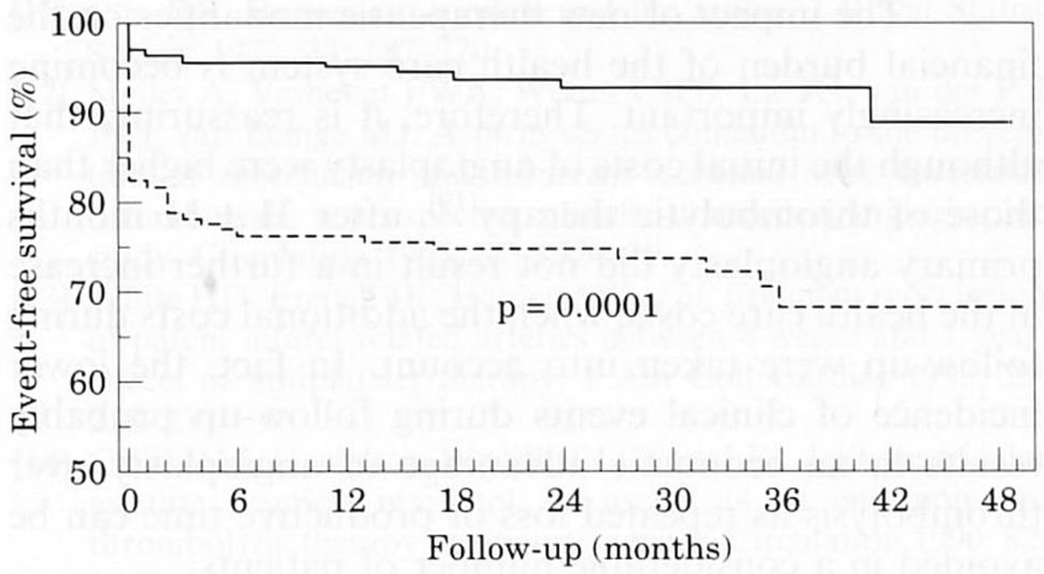

Figure 2 **Incidence of cardiac death or non-fatal recurrent myocardial infarction in 301 patients with acute myocardial infarction, randomized to treatment with streptokinase (– – –) or primary angioplasty (———) ($P< 0{\cdot}001$).**

group, $P=0{\cdot}002$. Many of these infarct-related vessels were found to be occluded at angiography. This explains the strong association between reinfarctions and patency of the infarct-related vessel, as shown in Table 3. Following the coronary angiogram that was used to assess patency of the infarct related vessel, the difference in reinfarction rate was also significant, 15 vs three, $P=0{\cdot}003$, in angioplasty patients and streptokinase patients, respectively. Eleven patients randomized to angioplasty had a non-fatal reinfarction or cardiac death (7%), compared to 42 patients (28%) randomized to streptokinase, $P<0{\cdot}001$, see also Fig. 2. The relative risk of the combination of cardiac death and non-fatal reinfarction of streptokinase patients compared to angioplasty patients is 4·3 (95% confidence interval 2·2–8·3). The influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy on reinfarction is shown in Table 3. Randomization to primary angioplasty was associated with a very low reinfarction rate.

Left ventricular ejection fraction was measured before hospital discharge in 98% of patients who survived the initial hospital phase. Patients randomized to angioplasty had an ejection fraction of $49 \pm 11\%$ compared to $44 \pm 11\%$ in patients randomized to streptokinase, $P<0{\cdot}001$. After a mean follow-up of 31 months, a left ventricular ejection fraction measurement was obtained in 95% of survivors. There was no relation between the time interval between first and second ejection fraction measurements and the results. Angioplasty patients had an ejection fraction of $48 \pm 12\%$ vs $43 \pm 13\%$ in streptokinase patients, $P=0{\cdot}006$. The ejection fraction of patients who died during follow-up was $32 \pm 16\%$ at hospital discharge. The effects of age, coronary anatomy, prior MI, infarct location and reperfusion therapy on left ventricular ejection fraction are shown in Table 4. Patency of the infarct-related vessel and previous infarctions were the most important determinants of left ventricular ejection fraction.

The total medical costs, including the initial hospital stay, readmissions, procedures such as angioplasty or bypass surgery, physician charges, and costs of

Table 4 Left ventricular ejection fraction : the influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy

	n	Discharge	n	follow up
Age <65	195	47 ± 11%	177	45 ± 12%
		ns		ns
Age <65	78	46 ± 12%	78	46 ± 13%
Patent IRV	225	48 ± 11%	201	47 ± 12%
		$P=0{\cdot}0012$		$P=0{\cdot}001$
Occluded IRV	64	43 ± 12%	54	40 ± 15%
SVD	117	49 ± 10%	106	48 ± 11%
		$P=0{\cdot}006$		$P=0{\cdot}0022$
MVD	169	45 ± 12%	147	43 ± 13%
Prev. MI	49	41 ± 14%	43	40 ± 14%
		$P<0{\cdot}0001$		$P=0{\cdot}0009$
No prev. MI	240	48 ± 10%	212	47 ± 12%
Ant. MI	137	43 ± 13%	122	43 ± 14%
		$P<0{\cdot}001$		$P=0{\cdot}0008$
Non-ant. MI	152	50 ± 9%	133	48 ± 10%
Streptokinase	140	44 ± 11%	123	43 ± 13
		$P<0{\cdot}0001$		$P=0{\cdot}0025$
Angioplasty	149	50 ± 11%	132	48 ± 12%

The differences between discharge EF and EF at follow-up were not significant. Abbreviations as in Table 2.

pharmacological therapy were Dfl.30 670 per patient for the angioplasty assigned patients and Dfl.30 382 per patient for the streptokinase patients. Recalculating the costs per survivor, the mean costs per patient amount to Dfl.33 299 per patient assigned to angioplasty and to Dfl.35 092 per patient assigned to streptokinase. If costs were calculated for event-free survivors, the costs were Dfl.34 028 for patients assigned to angioplasty compared to Dfl.43 114 for patients assigned to streptokinase therapy. The influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy on costs is shown in Table 5. Multivessel coronary artery disease and a previous myocardial infarction were associated with increased costs.

Discussion

This study shows that primary coronary angioplasty in patients with an acute myocardial infarction is associated with a lower incidence of cardiac death and recurrent infarction during follow-up. Furthermore, there was a sustained beneficial effect on left ventricular function. Compared to thrombolytic therapy, primary angioplasty did not result in an increase in medical costs. Patency of the infarct-related coronary artery was strongly related to clinical outcome and this explains the improved clinical outcome after angioplasty compared to thrombolytic therapy. In addition, the presence of multivessel disease, a history of a previous myocardial infarction and the location of the myocardial infarction were important determinants of clinical outcome and costs.

Table 5 Costs: the influence of age, coronary anatomy, prior MI, infarct location and reperfusion therapy

	n	Discharge	n	Follow up
Age <65	201	19094	195	30837
		ns	ns	
Age >65	100	17470	92	32607
Patent IRV	226	18294	225	30593
		ns		ns
Occluded IRV	75	19337	62	34348
SVD	117	18533	117	25773
		ns		$P=0{\cdot}0001$
MVD	179	18433	167	35655
Prev. MI	53	17656	49	37673
		ns		$P=0{\cdot}007$
No prev. MI	248	18746	238	30114
Ant. MI	154	18393	150	31304
		ns		ns
Non-ant. MI	147	18723	137	31514
Streptokinase	149	17985	138	31822
		ns		ns
Angioplasty	152	19112	149	31017

Abbreviations as in Table 2. Costs are total medical costs in Dfl.

The primary target of all reperfusion therapies is rapid and complete reopening of acutely occluded coronary arteries. This concept has recently been confirmed by the results of the GUSTO trial (Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded coronary arteries)[9]. Coronary patency, defined as the restoration of normal blood flow in the infarct-related vessel, results in myocardial salvage and improved survival. Patency rates achieved with primary angioplasty can currently not be obtained with thrombolytic agents[3–5,8,9]. Indeed, our data indicate that a higher patency rate of angioplasty patients compared to streptokinase patients results in a higher left ventricular ejection fraction, a reduced incidence of reinfarction and improved survival. This implies that thrombolytic agents or adjunctive therapies that would result in a higher rate of early and sustained TIMI 3 flow might offer similar benefit.

A second mechanism by which primary angioplasty results in a better long-term clinical outcome is the low incidence of reocclusion after successful angioplasty of less than 10%[8], compared to a reocclusion rate of 25–30% after successful reperfusion by thrombolytic agents[12,13].

The use of the left ventricular ejection fraction as an end point in trials of acute myocardial infarction has been surrounded by controversy[14,15]. Some investigators have shown relationships between early reperfusion or patency, and limitation of infarct size and/or left ventricular function[7,16] and long-term survival[17]. Our data strongly suggest that a higher, early and sustained patency rate of the infarct-related vessel results in a more preserved left ventricular function. This is probably in part through the influence of successful reperfusion on left ventricular remodelling[18].

The impact of new therapeutic modalities on the financial burden of the health care system is becoming increasingly important. Therefore, it is reassuring, that although the initial costs of angioplasty were higher than those of thrombolytic therapy[19], after 31 ± 11 months primary angioplasty did not result in a further increase in the health care costs, when the additional costs during follow-up were taken into account. In fact, the lower incidence of clinical events during follow-up probably results in an economic advantage of angioplasty over thrombolysis as repeated loss of productive time can be avoided in a considerable number of patients.

Conclusion

The benefits of primary angioplasty compared to thrombolytic therapy with intravenous streptokinase are sustained during follow-up without an increase in costs.

We are indebted to the many general practitioners of the region for their speedy referral of patients with acute myocardial infarction.

References

[1] ISIS-2 Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction. Lancet 1988; 2: 349–60.

[2] Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986; 1: 397–402.

[3] Granger CB, Califf RM, Topol EJ. Thrombolytic therapy for acute myocardial infarction. A review. Drugs 1992; 44: 293–325.

[4] Grines CL, Browne KF, Marco J *et al.* for the Primary Angioplasty in Myocardial Infarction Study group. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1993; 328: 673–9.

[5] 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: 680–4.

[6] Gibbons RJ, Holmes DR, Reeder GS, Bayley KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. N Engl J Med 1993; 328: 685–91.

[7] de Boer MJ, Suryapranata H, Hoorntje JCA *et al.* Limitation of infarct size and preservation of left ventricular function after primary coronary angioplasty compared with intravenous streptokinase in acute myocardial infarction. Circulation 1994; 90: 753–61.

[8] de Boer MJ, Reiber JHC, Suryapranata H, van den Brand MJBM, Hoorntje JCA, Zijlstra F. Angiographic findings and catheterisation laboratory events in patients with primary coronary angioplasty or streptokinase therapy for acute myocardial infarction. Eur Heart J 1995; 16: 1347–55.

[9] 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.

[10] Kaplan EL, Meier P, Nonparametric estimation from incomplete observations. J Am Statist Assoc 1958; 53: 457–81.

[11] Cox DR. Regression models and life tables. J Royal Statist Society 1972; 34: 187–220.
[12] Meijer A, Verheugt FWA, Werter CJPS, Lie KI, van der Pol JMJ, van Eenige MJ. Aspirin versus coumadin in the prevention of reocclusion and recurrent ischemia after successful thrombolysis: a prospective placebo-controlled angiographic study. Circulation 1993; 87: 1524–30.
[13] White HD, French JK, Hamer AW *et al.* Frequent reocclusion of patent infarct-related arteries between 4 weeks and 1 year: effects of antiplatelet therapy. J Am Coll Cardiol 1995; 25: 218–23.
[14] Califf RM, Harrelson-Woodlief L, Topol EJ. Left ventricular ejection fraction may not be useful as an end point of thrombolytic therapy comparative trials. Circulation 1990; 82: 1847–53.
[15] Morris RM, White HD. Therapeutic trials in coronary thrombosis should measure left ventricular function as primary end-point of treatment. Lancet 1988; 1: 104–6.
[16] Simoons ML, Serruys PW, van den Brand M *et al.* Early thrombolysis in acute myocardial infarction: Limitation of infarct size and improved survival. J Am Coll Cardiol 1986; 7: 717–28.
[17] Simoons ML, Vos J, Tijssen JGP *et al.* Long-term benefit of early thrombolytic therapy in patients with acute myocardial infarction: 5 year follow-up of a trial conducted by the interuniversity Cardiology Institute of the Netherlands. J Am Coll Cardiol 1988; 14: 1609–15.
[18] Kloner RA. Coronary angioplasty: a treatment option for left ventricular remodeling after myocardial infarction. J Am Coll Cardiol 1992; 20: 314–6.
[19] De Boer MJ, van Hout BA, Liem AL, Suryapranata H, Hoorntje JCA, Zijlstra F. A cost-effective analysis of primary coronary angioplasty versus thrombolysis for acute myocardial infarction. Am J Card 1995; 76: 830–33.

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