Comparison of Thrombolytic Therapy and Primary Coronary Angioplasty With Liberal Stenting for Inferior Myocardial Infarction With Precordial ST-Segment Depression

Immediate and Long-Term Results of a Randomized Study

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Objectives. **The aim of the study was to compare randomly assigned primary angioplasty and accelerated recombinant tissue plasminogen activator (rt-PA), in patients with "high-risk" inferior acute myocardial infarction (ST-segment elevation in the inferior leads and ST-segment depression in the precordial leads).**

Background. **The ST-segment depression in the precordial leads is a marker of severe prognosis in patients with inferior myocardial infarction. The comparative outcome of treatment with primary angioplasty or lysis with accelerated rt-PA has not been investigated.**

Methods. **One hundred and ten patients within 6 h of symptoms were randomized to either treatment. To assess the in-hospital and 1-year outcome of both treatments the following results were compared: death or nonfatal infarction, recurrence of angina, left ventricular ejection fraction (LVEF), and the need for repeat target vessel revascularization (TVR).**

Results. **In patients treated with angioplasty (55) and rt-PA (55) the rate of in-hospital mortality and reinfarction was 3.6% versus 9.1% ($p = 0.4$). Recurrence of angina was 1.8% versus 20% ($p = 0.002$), new TVR was used in 3.6% versus 29.1% ($p = 0.0003$), and the LVEF (%) at discharge was 55.2 ± 9.5 versus 48.2 ± 9.9 ($p = 0.0001$). There were no hemorrhagic strokes, no emergency coronary artery bypass graft (CABG) and identical (5.5%) need for blood transfusions. At 1 year, the incidence of death, reinfarction or repeat TVR was 11% in the percutaneous transluminal coronary angioplasty (PTCA) group versus 52.7% in the rt-PA group (log-rank 22.38, $p < 0.0001$).**

Conclusions. **Primary angioplasty is superior to accelerated rt-PA in terms of both myocardial preservation and reduction of in-hospital complications in patients with inferior myocardial infarction and precordial ST-segment depression. Primary angioplasty also yields a better long-term event-free survival.**

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Early restoration of a normal blood flow in the infarct-related artery (IRA) is the mechanism by which reperfusion therapy improves survival and related clinical outcomes in patients with acute myocardial infarction (AMI) (1–3). Clinical predictors of outcome in patients treated with thrombolysis have been identified in large studies (4). Although there is some evidence that treatment with percutaneous transluminal coronary angioplasty (PTCA) may be more beneficial than thrombolysis, particularly in higher-risk patients (5,6), the magnitude of both short- and long-term clinical benefits of PTCA is still inconsistent (7). The accurate identification of subgroups of patients with AMI who may benefit most from primary PTCA is important for the rational use of this demanding therapeutic option.

Inferior AMI is generally considered low-risk, and the relative benefit of reperfusion therapy may be viewed as substantially minor (8). However, concomitant precordial ST-segment depression, as observed in nearly 50% of patients with inferior AMI (8,9), is a predictor of a more severe prognosis. In the prethrombolytic era, the mortality of these patients was reported to be as high as 13% in hospital, and 11.3% within 1 year (10,11). The benefit of thrombolytic therapy becomes apparent in these patients when they are compared to those with ST-segment changes confined to the inferior leads (8,12). A recent analysis of data from patients with inferior AMI in the Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO) study has confirmed the higher rate of complications and mortality associated with precordial ST-segment depression (13). Although the importance of rapid and aggressive reperfusion therapy in

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Abbreviations and Acronyms

AMI	=	acute myocardial infarction
CABG	=	coronary artery bypass graft
CHF	=	congestive heart failure
GUSTO	=	The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes
IRA	=	infarct-related artery
LVEF	=	left ventricular ejection fraction
PTCA	=	percutaneous transluminal coronary angioplasty
rt-PA	=	recombinant tissue plasminogen activator
TIMI	=	Thrombolysis in Myocardial Infarction
TVR	=	target vessel revascularization

these patients is recognized (8,14,15), primary PTCA in this setting is not currently proposed as a superior treatment.

The aim of this study was to compare both the in-hospital and long-term results of treatment with either primary PTCA or thrombolysis using accelerated recombinant tissue plasminogen activator (rt-PA) in patients with inferior AMI and concomitant precordial ST-segment depression.

Methods

Study patients. *Inclusion criteria*. Male and female patients under the age of 80, presenting within 6 h of symptom onset (typical chest pain lasting more than 30 min) with ST-segment elevation >0.1 mV in at least two of the inferior leads, and concomitant precordial ST-segment depression in at least three precordial leads, the sum being >3 mm; this criterion was used to exclude small, low-risk, posterior AMI (15,16). Informed consent by the patient to participate in the study was a requisite for inclusion. *Exclusion criteria*. Formal contraindications to thrombolysis or to anticoagulation with heparin; cardiogenic shock or blood pressure <80 mm Hg (these patients are selectively treated with primary PTCA), and anticipated impossibility of percutaneous femoral vascular access.

Electrocardiographic analysis. The extent of ST-segment deviation was determined for all leads (measured at 60 ms after the J point relative to the TP segment). The sums of ST elevation in the inferior leads (D2-D3,aVF), lateral leads (V5-V6,D1,aVL), right ventricular leads (V3r,V4r), and of ST-segment depression in the anterior leads (V1 through V6) were annotated in all cases.

Randomization and treatment strategies. A brief clinical history was obtained during physical examination in the Emergency Department. Immediately after informed consent was obtained, the patients were randomized to one of the two treatment strategies. The elegibility of the patient for the study was assessed by the staff cardiologist on duty. Randomization was performed by means of sealed envelopes. When patients were allocated to primary PTCA, the emergency team of the Catheterization Unit was called. All patients received standard medical care, including aspirin 300 mg IV, ranitidine 50 mg IV, and nitroglycerin IV when indicated, without lowering systolic blood pressure <100 mm Hg; other cardiac medications and opiates for relief of pain were administered at the discretion of the physician. *Thrombolytic therapy* treatment was started in the Intensive Care Unit; the accelerated, weight-adjusted treatment with rt-PA was used in all patients randomized to lytic therapy, according to the GUSTO protocol (17). Heparin was administered immediately as a 5000-U IV bolus, followed by an initial infusion of 1000 U/h, which was subsequently adjusted to maintain the activated partial-thromboplastin time between two and three times the basal values for 48 h. *Successful thrombolysis* was intended as both the relief of ischemic chest pain and a reduction ≥50% in ST-segment elevation after 120 min of the rt-PA bolus. *Interruption of thrombolysis* was considered in case of severe hypotension, bleeding, holosystolic murmur, pulmonary edema, and left ventricular failure; *failed thrombolysis* was intended as the persistence of intense ischemic chest pain or <50% reduction in ST-segment elevation at 120 min of the rt-PA bolus; both these cases were indications for emergency catheterization, immediately followed by rescue PTCA if the IRA was occluded and suitable for the procedure.

Primary angioplasty. Patients were transported to the Catheterization Laboratory as soon as possible for coronary angiography (the Emergency Department and the Cardiac Catheterization Laboratory are attached structures, and the emergency team of the laboratory is on call around the clock). Immediately after coronary angiography, a bolus of 10,000 U of heparin was administered IV if PTCA was indicated, and an activated clotting time >300 s was maintained during the procedure. A prophylactic bolus of IV lidocaine (1 mg/kg) was also given before crossing the occlusion with the guide wire. The PTCA was performed with the conventional technique, and coronary stents were used without restrictions from the beginning of the study. Post-PTCA management included heparin infusion for 48 h prior to sheath removal, and antiplatelet therapy with ticlopidine 500 mg/day; the latter was begun immediately after the procedure, and continued for 1 month. The IRA was the only target of the procedure. In the presence of severe left main coronary artery stenosis, crossover to intracoronary thrombolysis, followed by urgent coronary artery bypass graft (CABG) surgery, was indicated only when the left circumflex was the IRA. In patients with spontaneous reperfusion of the IRA (TIMI [Thrombolysis in Myocardial Infarction] grade 3 flow), whether or not to perform the PTCA was the operator's choice. *Successful PTCA* was intended as TIMI grade 3 coronary flow in the IRA and a residual stenosis <50%, with relief of ischemic chest pain, and reduction ≥50% of ST-segment elevation, as compared to the preprocedure recording; the lack of any of these features was considered as *failed PTCA*, and crossover to intracoronary thrombolysis, with medical management or urgent CABG, was decided by the operator. Abciximab was not used in any patient in this study.

Unscheduled catheterization. This procedure was performed in cases of failure of thrombolysis or recurrence of ischemia. *Angiographic analysis*. Coronary angiography was

Table 1. Baseline Characteristics of the Two Groups

Characteristics	Primary PTCA Group (55)	rt-PA Group (55)	p Value
Prehospital delay (min)	152.5 ± 65.7 (25–355)	154.7 ± 69.6 (45–345)	0.9
In-hospital delay (min)	53.2 ± 11.7 (25–75)	36.5 ± 10.3 (21–90)	0.0001
Gender (males)	45 (82%)	47 (85%)	0.9
Age (years)	63.4 ± 8.4 (42–80)	60.2 ± 9.6 (36–80)	0.07
Diabetes	9 (16.3%)	6 (10.9%)	0.6
Current smokers	35 (63.6%)	30 (54.5%)	0.7
Hypertension	22 (40%)	25 (45.5%)	0.8
Hypercholesterolemia	20 (36.4%)	24 (43.6%)	0.7
Previous bypass surgery	4 (7.3%)	3 (5.5%)	0.9
Previous PTCA	1 (1.8%)	0	0.9
Previous myocardial infarction	10 (18.2%)	6 (10.9%)	0.5
Heart rate (beats/min)	69.0 ± 19.7	76.2 ± 16.5	0.04
Systolic blood pressure (mm Hg)	115.8 ± 29.9	121.8 ± 20.8	0.2

scheduled in all patients on the day before discharge, but it was performed at any time earlier if clinically indicated. The TIMI coronary flow grade and residual stenosis of the IRA, and the left ventricular ejection fraction (LVEF%) of patients in the two groups, were compared.

Clinical follow-up. A 6-month control visit was also scheduled in all patients. Elective interventions after discharge were indicated when patients reported symptoms or showed signs of myocardial ischemia. A telephone follow-up was also obtained at 12 months for each patient, and a medical examination was performed in all patients reporting new events.

Study end points. To assess the results of both treatment strategies, the following variables were compared: *A) During hospital stay*: 1A) death (from cardiac and noncardiac origin); 2A) reinfarction defined as chest pain, changes in the ST-T-segment, and a second increase in the creatine kinase level to more than twice the upper normal limit, or an increase of >200 U/l over the previous value if the level had not dropped to normal; 3A) recurrence of angina at rest with ST-segment changes; 4A) the need for new target vessel revascularization (TVR); 5A) nonfatal stroke; 6A) vascular or hemorrhagic complications needing blood transfusions; 7A) severe ventricular arrhythmia (tachycardia or fibrillation); 8A) congestive heart failure (CHF, Killip class ≥2); 9A) the angiographic result of both treatments at hospital discharge, in terms of LVEF, IRA patency, and residual stenosis (as assessed by Quantitative Coronary Analysis with Philips DCI, ACA package, release 1.1.2); 10A) peak creatine kinase (CK) level and time to peak; and 11A) the length of initial hospital stay. *B) During the follow-up period* the following variables were compared: 1B) death (from cardiac and noncardiac origin); 2B) reinfarction; 3B) recurrence of angina; 4B) new TVR and non-TVR; 5B) CHF needing hospital admission; and 6B) total new hospital admissions.

Statistical analysis. All end points were analyzed according to the principle of intention to treat. Continuous data are expressed as means and standard deviations; discrete variables are given as absolute values and percentages. The two-tailed Student's *t* test was used for comparison of parametric variables, and the chi-square test for discrete variables. Event-free survival analysis was performed using Kaplan-Meier curves (log-rank test). In case of multiple events (recurrence of angina, nonfatal reinfarction, death, and new admission for repeat TVR or CHF) only the first occurring event was considered.

The research protocol was reviewed and approved by the ethical board of our institution, and all the patients included in the study gave their informed consent.

Results

Patient characteristics at recruitment. Between December 1993 and December 1996, a total of 110 consecutive patients were enrolled and randomized to primary PTCA or thrombolysis; all of the 55 patients in each group received the assigned protocol treatment. During the study period, 9 additional patients with inferior AMI and precordial ST-segment depression were admitted within 6 h of onset, and were not randomized: 4 patients presented with systolic blood pressure <80 mm Hg or with cardiogenic shock, 3 were older than 80 years of age, 1 had contraindication to lysis, and another had no possibilities of femoral vascular access. The two groups were similar in terms of baseline characteristics, except for the heart rate at admission (Table 1). Mean in-hospital delay (from arrival at the Emergency Department to the beginning of assigned treatment) was 53.2 ± 11.7 min for PTCA and 36.5 ± 10.3 min for thrombolysis ($p = 0.0001$). In the PTCA group, reperfusion was achieved within 13.8 min of further delay; in the rt-PA group the actual time to reperfusion could not be assessed as early angiography was not performed. Analysis of the electrocardiographic (ECG) characteristics shows the similar presentation of patients from the two groups (Table 2); 64 patients (58.2%) had anterior ST-segment depression from V4 to V6, and 18 (16%) from V1 to V6. Concomitant right ventricular AMI was present in 35.5% of our patients.

Procedural and angiographic results. All patients assigned to the lytic therapy completed the treatment as specified in the

Table 2. Electrocardiographic Characteristics of the Two Groups

Electrocardiographic Presentation	Primary PTCA Group (55)	rt-PA Group (55)	p Value
Σ ST elevation in inferior leads (DII, DIII, aVF) (mm)	+8.0 ± 5.5	+8.0 ± 3.9	0.9
Σ ST elevation in lateral leads V5, V6, DI, aVL (mm)	+5.3 ± 4.2	+3.7 ± 4.2	0.4
Number of cases	6 (11%)	10 (18%)	0.3
Σ ST depression in precordial leads (V1 through V6) (mm)	−12.2 ± 7.6	−10.3 ± 6.7	0.2
Number of cases	9 (16%)	9 (16%)	
Σ ST depression from V1 to V3 (mm)	−6.9 ± 4.3	−5.8 ± 3.9	0.2
Number of cases	15 (27%)	13 (24%)	0.8
Σ ST depression from V4 to V6 (mm)	−5.2 ± 4.5	−4.2 ± 2.3	0.3
Number of cases	31 (57%)	33 (60%)	0.8
Σ ST elevation in V3-R (mm)	+0.65 ± 0.9	+0.55 ± 0.8	0.7
Number of cases	23 (42%)	16 (29%)	0.2

Abbreviations: Σ: sum.

protocol. Patients in the PTCA group showed an occluded IRA with TIMI grade 0–1 flow in 49 cases (89%), a TIMI grade 2 flow in 5 cases (9%), and a spontaneous reperfusion with TIMI grade 3 flow in 1 case (2%); all were treated with PTCA. Rescue PTCA of the occluded IRA after failed thrombolysis was indicated and was successfully performed in 2 patients. Emergency CABG was not required.

In all patients except one, PTCA was successful (98.2%); this patient had a TIMI grade 2 coronary flow with persistent ST elevation at the end of the procedure and was subsequently managed with medical therapy. Coronary stents were implanted in 32 patients (58%). Intraaortic balloon pumping was used in 5 patients (9%) in the PTCA group, and 2 (3.6%) in the lytic group. Angiographic data are shown in Table 3.

In-hospital medical management. In addition to heparin, IV nitrates were given to most patients during the first 48 h. The subsequent drug regimen used in both groups is listed in Table 4. The only significant difference was the protocol use of ticlopidine in patients treated with PTCA, except when specifically contraindicated.

Coronary and left ventricular angiography were performed before discharge in 51 patients treated with PTCA (92.7%) and in 52 treated with lytic therapy (94.5%). Angiography was not performed in 7 patients: this was due to the need for CABG (3 cases) or to death (2 cases) during hospital stay, to a local vascular complication during previous primary PTCA (1 case), and to refusal by the patient (1 case). Both the prevalence of multivessel disease and the distribution of the IRA were similar between groups. Coronary TIMI grade flow and residual stenosis in the IRA and LVEF were significantly better in the PTCA group than in the trombolysis group (Table 3).

In-hospital clinical outcome. In-hospital events are summarized in Table 5. The differences in mortality and reinfarction, despite a trend in favor of PTCA, did not reach statistical significance. In the PTCA group, one patient (1.8%) died after CABG following successful primary PTCA of a 14-year-old saphenous vein graft. One patient (1.8%) had reinfarction attributable to the occlusion of a coil stent; he was promptly treated with PTCA and had no other complications. One additional patient needed repeat PTCA for recurrence of angina at rest (1.8%), and 2 other patients were operated

Table 3. Angiographic Data of the Patient Groups

Angiographic Data	Primary PTCA Group (55)	rt-PA Group (52)	p Value
Infarct related artery			
RCA	49 (89%)	42 (81%)	0.2
LCx	6 (11%)	10 (19%)	0.4
One-vessel disease	27 (49%)	26 (50%)	0.8
Two-vessel disease	14 (25.5%)	17 (32.7%)	0.5
Three-vessel disease	14 (25.5%)	9 (17.3%)	0.2
Angiographic findings at discharge			
TIMI flow grade			
0–1	—	15 (28.8%)	0.0001
2	—	6 (11.6%)	0.01
3	51 (100%)	31 (59.6%)	0.0001
Residual stenosis (%)	20.7 ± 13.4 (0–31)	74.6 ± 24.7 (4–100)	0.001
Left ventricular ejection fraction (%)	55.2 ± 9.5 (35–85)	48.2 ± 9.9 (28–68)	0.0001

Abbreviations: Lcx: left circumflex; RCA: right coronary artery.

Table 4. Medical Therapy

In-Hospital Medical Therapy	Primary PTCA Group (55)	rt-PA Group (55)	p Value
Aspirin	6 (11%)	42 (72%)	0.0001
Ticlopidine	49 (90%)	13 (24%)	0.0001
Nitrate (oral)	20 (36%)	25 (45%)	0.6
Nitrate (IV)	29 (36%)	14 (25%)	0.4
Beta-blocker (oral)	35 (64%)	37 (67%)	0.9
Agiotensin-converting-enzyme inhibitors	18 (33%)	22 (40%)	0.7
Calcium-channel-blocker	10 (18%)	11 (20%)	0.9
Statin	8 (15%)	7 (13%)	0.9

before hospital discharge owing to severe left main coronary artery disease. Three patients from the lytic group (5.5%) died from recurrent AMI, 2 patients sustained a nonfatal reinfarction (total reinfarction 9.1%) and 11 had recurrence of angina at rest. The PTCA was performed successfully in 2 patients as a rescue procedure for failed thrombolysis, in 1 patient with reinfarction, in 7 patients with recurrence of angina, in 2 patients with a positive stress test before discharge despite medical therapy, and in 3 patients electively at discharge due to preference of the physician. Two patients with unstable symptoms had CABG before discharge due to left main coronary artery disease in one case, and to severe multivessel disease with post-AMI mitral regurgitation in the other.

Overall, a new TVR was needed in 3.6% of patients of the PTCA group (2 repeat PTCA), versus 29.1% in the rt-PA group (15 PTCA and 1 CABG) ($p = 0.0003$). A non-TVR was indicated in 2 patients (3.6%) in the PTCA group, and in 1 patient (1.8%) in the thrombolysis group.

The LVEF% at discharge was significantly better in the PTCA arm. No patient had intracerebral bleeding, and the need for blood transfusion was identical in the two groups. Patients initially treated with thrombolysis had higher (although nonsignificant) peak CK levels, with longer time to peak. They also had a higher incidence of CHF. The length of hospital stay was longer in patients initially treated with thrombolysis ($p = 0.0001$).

Follow-up results. No event was observed during the first month after discharge. During the first semester one patient randomized to PTCA was readmitted for reinfarction and was treated medically, and one needed repeat TVR for recurrence of angina at rest due to in-stent restenosis. In the rt-PA group one patient died 3 months after CABG, and eight patients received a new TVR because of recurrence of angina (4 cases), and to the presence of effort ischemia (4 cases) ($p = 0.01$). Nine additional patients from the rt-PA group received elective CABG because of multivessel disease and impaired left ventricular function.

The cumulative incidence of events occurring in the first year after randomization is shown in Table 6. Figures 1 and 2 show the incidence of death or reinfarction, and of death, reinfarction or repeat TVR in both groups, as a Kaplan-Meier 1-year event-free survival curve. Recurrence of ischemia (reinfarction and angina) was observed in 4 patients (7.3%) in the PTCA group, and in 23 patients (41.8%) in the rt-PA group ($p = 0.0001$). Considering a composite outcome of death, nonfatal reinfarction, recurrence of angina, and CHF needing

Table 5. In-Hospital Clinical Outcome

Events	Primary PTCA Group (55)	rt-PA Group (55)	p Value
Death	1 (1.8%)	3 (5.5%)	0.6
Reinfarction (total)	1 (1.8%)	5 (9.1%) (3 fatal)	0.2
Death or nonfatal reinfarction	2 (3.6%)	5 (9.1%)	0.4
Recurrent angina at rest	1 (1.8%)	11 (20%)	0.002
Reinfarction or angina at rest	2 (3.6%)	16 (29.1%)	0.0003
Unscheduled catheterization	2 (3.6%)	14 (25%)	0.01
PTCA in hospital	55	15 (27.3%)	—
Bypass surgery in hospital	3 (5.5%)	2 (3.6%)	0.6
Target vessel revascularization	2 (3.6%)	16 (29.1%)	0.0003
Nontarget vessel revascularization	2 (3.6%)	1 (1.8%)	0.5
Stroke	0	0	
Bleeding (transfusion needed)	3 (5.5%)	3 (5.5%)	
Advanced A-V block	6 (11%)	4 (7.3%)	0.7
Ventricular tachycardia/fibrillation	4 (7.3%)	10 (18%)	0.1
Killip class ≥2	3 (5.5%)	10 (18%)	0.04
Peak CPK level (μl)	1902 ± 1298 (200–4,975)	2432 ± 1611 (341–6,890)	0.07
MB fraction	446 ± 430 (39–896)	488 ± 505 (41–234)	0.6
Time to CPK peak (h)	8.8 ± 3.7 (5–24)	12.6 ± 4.2 (3–24)	0.0001
Length of hospital stay (days)	9.2 ± 2.5 (4–15)	12.4 ± 3.7 (6–28)	0.0001

Table 6. One-year Follow-up From Admission (110 Patients)

Events	Primary PTCA Group (55)	rt-PA Group (55)	p Value
Time to follow-up (days)	344 ± 82 (28–1,213)	329 ± 106 (6–1,104)	0.4
Death	2 (3.6%)	4 (7.3%)	0.7
Reinfarction (total)	2 (3.6%)	5 (9.1%) (3 fatal)	0.4
Death or nonfatal reinfarction	4 (7.3%)	6 (11%)	0.7
Recurrence of angina	2 (3.6%)	18 (32.7%)	0.0001
Target vessel revascularization	3 (5.5%)	25 (45.5%)	0.0001
Nontarget vessel revascularization	2 (3.6%)	10 (18%)	0.03
PTCA after randomization	3 (5.5%)	24 (43.6%)	0.0001
Bypass surgery after randomization	3 (5.5%)	11 (20%)	0.05
CHF needing hospitalization	2 (3.6%)	1 (1.8%)	0.5
Hospital readmissions total	4 (7.3%)	21 (38.2)	0.0001

hospitalization in the first year after randomization, the event-free survival was 85.5% in the PTCA group (47/55 patients) versus 54.5% in the thrombolytic group (30/55 patients), odds ratio 0.32, 95% CI: 0.16 to 0.65; p = 0.0004.

Discussion

Prior studies have demonstrated that, at selected centers, primary PTCA in patients with AMI can achieve prompt and complete reperfusion of the IRA in nearly every case; it also provides valuable angiographic information whereby the best therapeutic strategy can be immediately tailored to each patient. Primary PTCA, however, is a logistically demanding technique, and IV thrombolysis remains the standard treatment for most patients because of its widespread availability and its use in a large number of studies in the last decade, along with proof that it reduces mortality (17–20). Although data from very recent trials suggest that primary PTCA may also be more beneficial than thrombolysis in low-risk patients (7,21), acceptance of primary PTCA as the treatment of choice for patients with AMI (22) is most likely to be gained through risk/benefit comparison with thrombolysis in higher-risk patients, such as those with anterior AMI, older age, heart rate >100 and cardiogenic shock (5,6,23).

Our study has compared the immediate and long-term results of primary PTCA and accelerated rt-PA in patients with inferior AMI and concomitant precordial ST-segment depression. Only two other randomized studies comparing PTCA with this thrombolytic regimen have been performed so far (7,24), and no randomized study is available in this subset of patients.

The clinical presentation of patients with inferior AMI and precordial ST-segment depression often fails to meet the above-mentioned "high-risk" criteria, whereas right ventricular involvement, advanced atrioventricular block, hemodynamically significant mitral regurgitation, and life-threatening arrhythmias are frequently observed in these patients and portend a severe prognosis (25–29). A recent analysis of results from the GUSTO-I trial in 16,521 patients with inferior AMI has confirmed that those with precordial ST-segment depression have larger infarctions, with a higher rate of complications

Figure 1. Kaplan-Meier curve of survival and freedom from death or reinfarction in the study patients, within 365 days after randomization, according to treatment group. Log rank 0.43, p = 0.5.

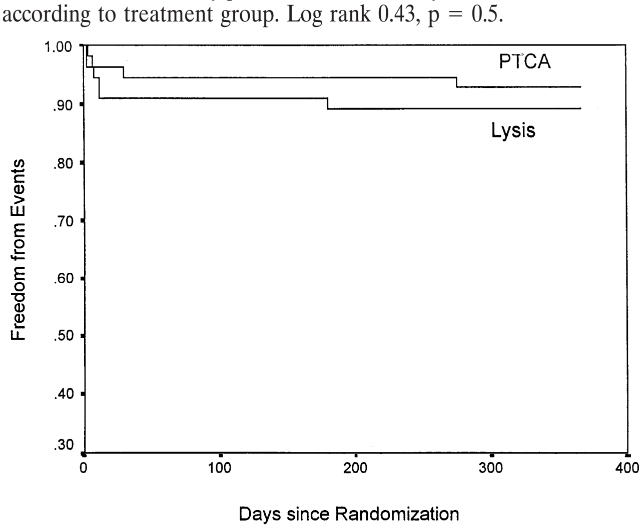
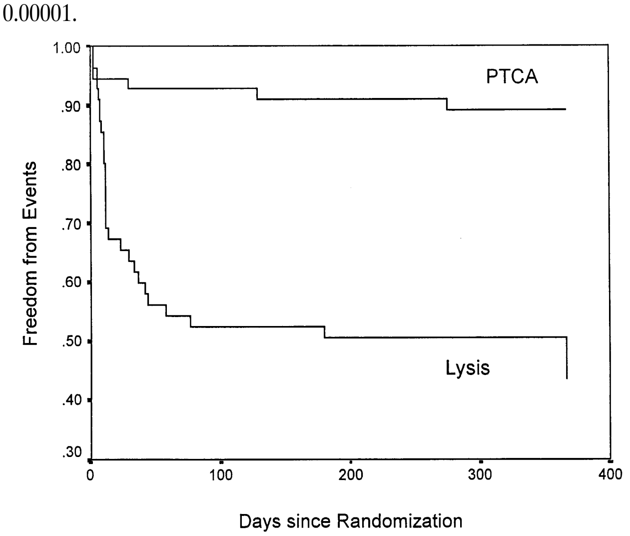


Figure 2. Kaplan-Meier curve of survival and freedom from death, reinfarction or repeat TVR in the study patients, within 365 days after randomization, according to treatment group. Log rank 22.38, p = 0.00001.



and a higher mortality over both the short and long term; the magnitude of precordial ST-segment depression is also reported to be an independent prognostic indicator for mortality at 1 month in these patients (13). Our cohort fits high-risk criteria for inferior AMI; in fact, patients with a precordial ST-segment depression <4 mm limited to leads V1-V3 are reported to have a better prognosis (13,16) and were not included; in addition, one-third of our patients had right ventricular involvement, which is a predictor of failed reperfusion by thrombolysis (30) and augmented in-hospital mortality (25,26).

Our study confirms the high immediate success rate of primary PTCA (5,31–33) also in this group of patients; the unrestricted use of coronary stents in our cohort may have contributed to this result (34). In comparison to other randomized trials, our results among patients treated with thrombolysis were similar to those obtained with the use of the same lytic protocol (7). The time necessary to start treatment with PTCA in our patients was longer than the time needed to begin thrombolysis, but the additional delay required to reestablish a normal coronary flow with PTCA was short (5,31,32).

In-hospital mortality and reinfarction. Both mortality and reinfarction rates in our patients treated with primary PTCA were lower than in those treated with thrombolysis, although the differences (1.8 vs. 5.5%, and 1.8 vs. 9.1%, respectively) were not significant. According to a recent meta-analysis comparing the results of all randomized trials of primary PTCA versus thrombolysis, the former has been shown to reduce the acute mortality by 34% as compared to the latter, with an estimated gain of about 21 lives saved per 1,000 patients treated (35). Nearly one-third of the mortality difference favoring PTCA, however, may be due to the higher incidence of hemorrhagic stroke after thrombolysis (5,21,35). Intracranial hemorrhage was not observed in our patients.

Early recurrence of ischemia and TVR. In our patients treated with primary PTCA, recurrent angina at rest during initial hospital stay was significantly less frequent than in those treated with thrombolysis (1.8 vs. 20%), as were both unscheduled cardiac catheterization (3.6 vs. 25%) and TVR (3.6 vs. 29.1%); as a consequence, the duration of hospital stay was also significantly shorter (9.2 vs. 12.4 days). This confirms the results of the primary angioplasty in myocardial infarction (PAMI) trial substudy in nonanterior AMI (6), with extension to our special subset of patients; the use of repeat TVR during hospital stay after initial thrombolysis in our cohort was only slightly lower than 36%, as reported in that trial (5).

Patency of the IRA and left ventricular function at discharge. As compared to our patients treated with thrombolysis, those treated with primary PTCA had both a significantly higher IRA patency (TIMI grade 3 flow in 100 vs. 59.6%) and a better preserved left ventricular function; this was reflected by a higher LVEF (55 vs. 48%) at predischarge coronary angiography, as well as by a lower incidence of CHF (5.5 vs. 18%). Similarly favorable results after primary PTCA in comparison to thrombolysis with streptokinase have been reported by Zijlstra et al. (31) at discharge, and also at 6-month follow-up in a cohort of nonanterior AMI patients (21). Our data confirm that primary PTCA yields superior IRA patency and LVEF preservation at discharge in patients with inferior AMI and precordial ST-segment depression, and we extend this observation to comparison with accelerated t-PA.

Long-term follow-up. In the year following randomization, both the recurrence of angina or reinfarction (7.3%) and the use of new interventions (11%) among our PTCA patients were infrequent, although data from this study are difficult to compare with others (36). The use of coronary stents may have improved the outcome of PTCA also in the follow-up, when the advantages of balloon reperfusion over thrombolysis seem to diminish (7). Myocardial revascularization was often performed in our patients after initial treatment with thrombolysis (31% before hospital discharge, and 62% within 6 months). This attitude in our center explains the high rate of new interventions and hospital readmissions in these patients, and this may have contributed to their good long-term survival. Figure 1 shows that differences in event-free survival between groups were minimal beyond the 6th month. In fact, by that time 62% of patients initially treated with thrombolysis had received a revascularization procedure, either complete with bypass surgery (20%), or limited to the culprit lesion with PTCA (42%); this "homogenization" of the sample obtained by the use of invasive procedures after thrombolysis may account for the fact that, at long term, death and reinfarction were infrequent in both arms of this trial, as observed in other studies (37).

Conclusions. Our study shows that primary PTCA with unrestricted use of stents yields a particularly favorable outcome, both over the short and long term in patients with inferior AMI and precordial ST-segment depression, as compared to thrombolysis with accelerated t-PA, in terms of both myocardial salvage, and recurrent ischemia with subsequent need for revascularization procedures.

Study limitations. The sample size of this single-center investigation was limited, and this may be responsible for the differences observed in the baseline characteristics of patients in the two patient groups, despite randomization. Our study was not powered to detect differences in mortality or reinfarction between the two groups. As a result, the trends observed in this regard favoring PTCA in this subset of patients require confirmation by larger studies, with use of both an independent angiographic core-laboratory, and a committee for the attribution of events—neither one of which was available for this single-center trial.

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