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Decreasing Hospital Mortality Between 1994 and 1998 in Patients With Acute Myocardial Infarction Treated With Primary Angioplasty but Not in Patients Treated With Intravenous Thrombolysis

Results From the Pooled Data of the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Registry and the Myocardial Infarction Registry (MIR)

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OBJECTIVES We investigated changes in the clinical outcome of primary angioplasty and thrombolysis for the treatment of acute myocardial infarction (AMI) from 1994 to 1998.

BACKGROUND Primary angioplasty for the treatment of AMI is a sophisticated technical procedure that requires experienced personnel and optimized hospital logistics. Growing experience with primary angioplasty in clinical routine and new adjunctive therapies may have improved the outcome over the years.

METHODS The pooled data of two German AMI registries: the Maximal Individual Therapy in AMI (MITRA) study and the Myocardial Infarction Registry (MIR) were analyzed.

RESULTS Of 10,118 lytic eligible patients with AMI, 1,385 (13.7%) were treated with primary angioplasty, and 8,733 (86.3%) received intravenous thrombolysis. Patients characteristics were quite balanced between the two treatment groups, but there was a higher proportion of patients with a prehospital delay of >6 h in those treated with primary angioplasty. The proportion of an in-hospital delay of more than 90 min significantly decreased in patients treated with primary angioplasty over the years (p for trend = 0.015, multivariate odds ratio [OR] for each year of the observation period = 0.84, 95% confidence interval [CI]: 0.73–0.96) but did not change significantly in patients treated with thrombolysis. Hospital mortality decreased significantly in the primary angioplasty group (p = 0.003 for trend; multivariate OR for each year = 0.73, 95% CI: 0.58– 0.93). However, for patients treated with thrombolysis, hospital mortality did not change significantly (p for trend 0.175, multivariate OR for each year: 1.02, 95% CI: 0.94– 1.11).

CONCLUSIONS Compared with thrombolysis the clinical results of primary angioplasty for the treatment of AMI improved from 1994 to 1998. This indicates a beneficial effect of the growing experience and optimized hospital logistics of this technique over the years. (J Am Coll Cardiol 2000; 36:2064–71) © 2000 by the American College of Cardiology

Randomized controlled trials that compared primary percutaneous transluminal coronary angioplasty with thrombolysis have shown that primary angioplasty is more effective than intravenous thrombolysis in reducing mortality and morbidity in patients with acute myocardial infarction (AMI) (1–6). However, concern persisted as to whether the results of highly specialized centers could be applied to clinical practice. Three myocardial infarction registries, the Myocardial Infarction Triage Investigators (MITI) Registry (7), the National Registry of Myocardial Infarction-2 (NRMI-2) (8) and a French registry (9), failed to show an advantage of primary angioplasty compared with treatment with thrombolysis in the "real world." Only a more recent registry (10) showed a more beneficial outcome with primary angioplasty compared with thrombolysis in a clinical routine setting at 271 hospitals in Germany. The reasons for this difference between the registries have not been studied yet.

The results of primary angioplasty are related to the experience of the performing physician (11–13). The introduction of stents (14–20) and IIb/IIIa receptor antagonists (21–23) in combination with primary angioplasty might have improved the outcomes of primary angioplasty. However, treatment with thrombolysis has not changed very

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Abbreviations and Acronyms

ACE	=	angiotensin-converting enzyme
AMI	=	acute myocardial infarction
CI	=	confidence interval
MIR	=	Myocardial Infarction Registry
MITI	=	Myocardial Infarction Triage Investigators Registry
MITRA	=	Maximal Individual Therapy in Acute Myocardial Infarction Registry
NRMI-2 registry	=	National Registry of Myocardial Infarction-2
OR	=	odds ratio

much over the last 15 years, with the exception of the introduction of tissue plasminogen activator (24).

In order to investigate changes in clinical outcome of primary angioplasty and thrombolysis from 1994 to 1998 in patients with AMI, we analyzed the pooled data of two German myocardial infarction registries: the Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) study (25,26) and the Myocardial Infarction Registry (MIR) (27).

METHODS

The MITRA study and the MIR were German prospective multicenter observational studies of the current treatment of AMI. The MITRA study recruited patients between June 1994 and January 1997. Fifty-four hospitals, mainly located in the southwest of Germany, including university hospitals, tertiary care centers and smaller hospitals, participated in the study. The MIR study was a nationwide registry that included patients from December 1996 to May 1998. A total of 217 hospitals, mainly community hospitals, participated. The protocols of both studies were almost identical. No hospital participated in both studies. Therefore, we used the pooled data from both studies for this analysis. All patients presenting within the first 96 h of the onset of pain were registered prospectively, as soon as the diagnosis of AMI had been made.

Reperfusion therapy. The following protocols for intravenous thrombolysis were suggested: intravenous application of 1.5 million U of streptokinase over 1 h or tissue plasminogen activator at a dose of 100 mg over 1.5 h intravenously. Angioplasty was performed according to the standard protocol of each center. The decision regarding the type of treatment was left to the discretion of the treating physician and not to the study protocol.

Definitions. Acute myocardial infarction was diagnosed in the presence of the two following criteria: persistent angina pectoris for ≥20 min and ST segment elevation of ≥1 mm in at least 2 standard leads or ≥2 mm in at least 2 contiguous precordial leads or the presence of a left bundle branch block. It was later confirmed by the elevation of cardiac enzymes of more than twice the normal upper range. Prehospital delay was defined as the time from the onset of symptoms until hospital admission. In-hospital delay was defined as the time from admission to the hospital until the start of primary angioplasty (angiographic needle entry = door-to-needle entry time) or the start of the infusion of the thrombolytic agent (door-to-needle time). A combined clinical end point was defined by the occurrence of death or reinfarction.

In this analysis only lytic eligible patients, that is, patients without contraindications against thrombolysis, treated with either primary angioplasty or intravenous thrombolysis and a prehospital delay of no longer than 12 h were included. Contraindications for thrombolysis were defined as stroke within the last 3 months, surgery or trauma within the last 14 days or active bleeding.

Statistics. DATA COLLECTION. Data of the prehospital period and the early intrahospital period (48 h) were collected within the first two to three days at the intensive care unit. Clinical events of the following hospital stay were reported on a separate record form at hospital discharge. Every participating center was committed by written consent to include each patient with AMI during the study period. The patients gave informed consent for processing of their anonymous data. All data sheets were sent to the central data processing center (Department of Cardiology, Herzzentrum Ludwigshafen) for uniform monitoring and registration.

DATA ANALYSIS. Absolute numbers, percentages and medians were computed to describe the patient population. Categorical values were compared by chi-square analysis or Fisher exact test as appropriate. Continuous variables were compared by two-tailed Wilcoxon rank sum test. The Cochran-Armitage trend test was used to analyze trends in proportions. Multiple logistic regression analysis was used to adjust for factors influencing hospital mortality, reinfarction and the combined end point during different years. Multiple logistic regression analysis was also performed for patients treated with primary angioplasty and for patients treated with thrombolysis to look for changes of the results of each therapy over the years. The following variables were examined: age, gender, location of infarction, prevalence of cardiogenic shock, previous myocardial infarction, resuscitation, heart failure at admission and the type of revascularization or the year of the recruitment. The presence of cardiogenic shock and resuscitation were not registered in 1994. Therefore, these parameters could not be included in the regression analysis of this year. p values < 0.05 were considered statistically significant. All p values are the results of two-tailed tests. The tests were performed using the SAS statistical package, version 6.12 (Cary, North Carolina).

RESULTS

During 1994 and 1998 10,118 patients with AMI, a prehospital delay ≤12 h and no contraindication for throm-

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Table 1. Patients Characteristics and Concomitant Medication Stratified by Year of Treatment in Patients Treated With Primary Angioplasty Compared With Patients Treated With Thrombolysis

	Year of Treatment									
	1994		1995		1996		1997		1998	
	pPTCA n = 36 (%)	Lysis n = 532 (%)	pPTCA n = 189 (%)	Lysis n = 1,139 (%)	pPTCA n = 182 (%)	Lysis n = 1,154 (%)	pPTCA n = 664 (%)	Lysis n = 4,599 (%)	pPTCA n = 314 (%)	Lysis n = 1,309 (%)
Age (years)	60	63	62	64	62	63	62	64‡	63	64
Men	72.2	69.7	69.8	71.3	80.2	72.6†	74.1	72.2	74.9	69.6
Anterior wall MI	52.8	49.6	46	48.8	44.1	48.1	48	47.2	48.3	47.3
Heart rate (1/min)	78	80	78	79	78	78	78.5	77	78	77
Previous MI	36.1	16.9‡	19.8	15.4	17	13.8	17.9	13.8‡	13.1	14.1
Heart failure at ad.	0	4.9	3.2	5.5	1.1	4.9†	2.3	5.5§	4.1	5.4
Resuscitation	*	*	7.9	7.4	4.4	7.5	6.2	7.1	7.6	7.9
Cardiogenic shock	*	*	6.2	4.2	2.8	3.2	4.7	4.4	6.7	3.7†
Ph delay (min)	120	120	130	120†	150	120‡	165	120§	150	125§
Ih delay (min)	84	30§	65	30§	90	30§	70	30§	67	30§
Concomitant medication, initiated during the first 48 h after admission:										
Aspirin	94.4	94.2	95.2	97.7†	99.5	98.6	97.3	95.5	97.4	96.7
Beta-blockers	47.2	38.9	67.7	60.1†	66.9	66.2	69.7	65.7†	74.8	69.8
ACE inhibitors	36.1	12.8§	66.1	55.8§	68.7	62.2	62.1	57.5†	69.6	64.4‡

*Not evaluated in 1994; †$p < 0.05$; ‡$p < 0.01$; §$p < 0.001$.
ACE = angiotensin converting enzyme; ad. = admission; ih delay = in-hospital delay, that is "door to needle-entry", or "door to needle"-time; Lysis = thrombolysis; MI = myocardial infarction; ph delay = prehospital delay; pPTCA = primary angioplasty.

bolysis who were treated with either primary angioplasty or thrombolysis were recruited by the MITRA and MIR registries. Of these patients, 1,385 (13.7%) were treated with primary angioplasty, and 8,733 (86.3%) received intravenous thrombolysis.

Patients characteristics and concomitant medication. Patients characteristics and concomitant medication initiated within the first 48 h after admission are shown in Table 1. Prehospital delays increased over the years in patients treated with primary angioplasty but not in patients treated with thrombolysis. This was caused by an increase in the proportion of patients with a prehospital delay >6 h in the primary angioplasty group (5.6% in 1994 to 12.1% in 1998). There was a higher proportion of patients with prior myocardial infarction and a lower rate of patients with heart failure at admission for patients treated with primary angioplasty compared with those treated with thrombolysis. Door-to-needle times for thrombolysis were always shorter than the in-hospital delay until the start of primary angioplasty. However, the proportion of an in-hospital delay of more than 90 min significantly decreased in patients treated with primary angioplasty over the years (p for trend = 0.015, multivariate analysis: odds ratio [OR] for each year: OR = 0.84, 95% confidence interval [CI]: 0.73 to 0.96). In both treatment groups the use of beta-adrenergic blocking agents and angiotensin-converting enzyme (ACE) inhibitors increased over the years. The use of aspirin and beta-blockers was not much different between the two treatment groups. However, patients treated with primary angioplasty were always more likely to receive ACE inhibitors.

Clinical events during 1994 to 1998. Hospital mortality decreased significantly from 1994 to 1998 in patients treated with primary angioplasty (p = 0.003 for trend) (Table 2, Fig. 1). This was confirmed by multiple logistic regression analysis after adjustment for other confounding parameters, showing an independent association of each following year with a lower mortality (OR = 0.73, 95% CI: 0.58 to 0.93). The reinfarction rate (p for trend 0.001, multivariate analysis: OR for each year: 0.56, 95% CI: 0.39 to 0.81), and the rate of the combined end point of death or reinfarction decreased significantly from 1994 to 1998 (p for trend = 0.001, multivariate analysis: OR for each year = 0.70, 95% CI: 0.56 to 0.86) (Table 2).

For patients treated with thrombolysis, neither hospital mortality (p for trend 0.175, multivariate analysis: OR for each year: 1.02, 95% CI: 0.94 to 1.11, Fig. 1) nor the reinfarction rate (p for trend 0.937; multivariate analysis: OR for each year: OR = 1.09, 95% CI: 0.97 to 1.23) or the rate of the combined end point of death or reinfarction (p for trend 0.182; multivariate OR for each year: 1.05, 95% CI: 0.97to 1.13, Table 2) changed significantly over the years.

When we compared the results of primary angioplasty with those of thrombolysis for each year, we found a continuously increasing benefit associated with primary angioplasty from 1994 to 1998. This benefit reached statistical significance in 1997 and 1998 for hospital mortality,

Table 2. Clinical Events Stratified by Year of Treatment in Patients Treated With Primary Angioplasty Compared With Patients Treated With Thrombolysis

	Year of Treatment													
	1994		1995		1996		1997		1998		p Value for Trend	
	pPTCA n = 36 (%)	Lysis n = 532 (%)	pPTCA n = 189 (%)	Lysis n = 1,139 (%)	pPTCA n = 182 (%)	Lysis n = 1,154 (%)	pPTCA n = 664 (%)	Lysis n = 4,599 (%)	pPTCA n = 314 (%)	Lysis n = 1,309 (%)	pPTCA	Lysis
Hospital mortality	13.9	10.2	9.5	12.4	6	9.9	6.1	11.9*	3.8	12.7*	0.003	0.175
Reinfarction	0	6.4	5.8	5.0	3.3	4	1.8	5.4*	1	5.4*	0.004	0.937
Death or reinfarction	13.9	15.0	13.2	15.7	8.8	12.9	7.5	15.7*	4.8	16.8*	0.001	0.182

pPTCA = primary angioplasty; lysis = thrombolysis.
*$p < 0.001$.

reinfarction and the combined end point (univariate analysis: Table 2; multivariate analysis: Fig. 2 and 3).

DISCUSSION

Many studies showed a declining mortality from coronary heart disease in the U.S. (28–31) and Western Europe (32) over the last 20 years. This reduction in mortality is assumed to be due to a declining incidence of myocardial infarction in the population and an improved survival of patients with myocardial infarction. The improved case fatality rates seem to be mainly attributable to the increasing use of reperfusion therapy (thrombolysis or primary angioplasty) and adjunctive medical therapy such as antiplatelet therapy, beta-blockers and ACE inhibitors. To the best of our knowledge, there are no data in the literature on changes in mortality in thrombolysis-eligible patients treated with either thrombolysis or primary angioplasty.

Selection of patients and patterns of treatment. The distribution of high-risk patients seemed to be balanced between the two treatment groups. There was no major difference in the age of the patients. Patients treated with primary angioplasty were more likely to have a prior myocardial infarction, and patients treated with thrombolysis more often showed signs of heart failure at admission. Important differences were seen in pre- and in-hospital delays. Compared with thrombolysis primary angioplasty was more often used in patients presenting with a prehospital delay of more than 6 h. This preference for primary angioplasty for patients with longer prehospital delays may result from differences between the hospitals with angioplasty facilities and those hospitals without such facilities. Hospitals with a catheterization laboratory are usually bigger than those without and are more likely to have cardiologists on call. Treatment by specialists may result in a better adherence to current recommendations (33,34), which advise the use of reperfusion therapy for up to 12 h after the onset of symptoms for patients with AMI (35). The beneficial effect of thrombolysis compared with no reperfusion therapy decreases with increasing prehospital delay (36). This may not be true in the same amount for primary angioplasty (37,38). This observation may also have contributed to the more liberal use of primary angioplasty for patients with longer prehospital delays.

Median in-hospital time to treatment was about 40 to 60 min longer for primary angioplasty than it was for thrombolysis. However, these "door to needle-entry" times for primary angioplasty were within 90 min, as recommended by the American Cardiac Societies.

Although adjunctive therapy within the first 48 h after admission with aspirin, beta-blockers and ACE inhibitors increased in both treatment groups over the years, patients treated with primary angioplasty were still more likely to be treated with ACE inhibitors. This may be mainly attributable to differences between hospitals as mentioned above.

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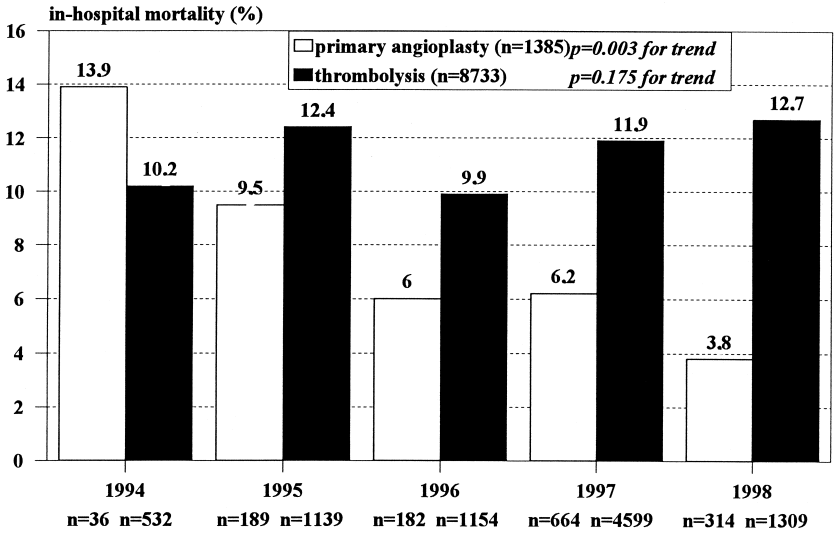

Figure 1. Hospital mortality in patients treated with primary angioplasty or thrombolysis from 1994 to 1998.

Hospital events. Hospital mortality, reinfarction rate and the combined end point of death or reinfarction decreased significantly in patients treated with primary angioplasty from 1994 to 1998, even after adjustment for confounding parameters. Hospital mortality decreased from 13.9% in 1994 to 3.8% in 1998 (p for trend = 0.001, multivariate analysis: OR for each year: OR = 0.73, 95% CI: 0.58 to 0.93). There were no significant changes in outcome for patients treated with thrombolysis.

In the MITRA/MIR registries mortality for patients treated with primary angioplasty in 1994 and 1995 was higher (13.9% and 9.5%) compared with that of other primary angioplasty studies (5.2% to 9.2%) (4,6–9,39), but mortality decreased in the following years. Mortality in patients treated with thrombolysis (11.3%) was constantly higher than the mortality reported by these other studies (5.4% to 7.6%). This difference in mortality between the MTRA/MIR and the other studies may be caused by different patient selection. In the MITRA/MIR studies patients in cardiogenic shock were not excluded. Patients were three years older, and anterior wall infarctions occurred more often compared with the NRMI-2 registry (8).

Thrombolysis has not changed very much over the last 15 years with the exception of the introduction of tissue plasminogen activator, which was demonstrated to be slightly superior to streptokinase (about 1% absolute risk reduction) (24). Therefore, the nearly constant mortality rate in these patients was not surprising.

Primary angioplasty, however, is not such an easy-to-perform therapy as thrombolysis. The results of primary angioplasty strongly depend on the experience of the physician, a well-trained catheterization team and optimal hospital logistics to keep in-hospital times as short as possible. All those factors have proven to influence the

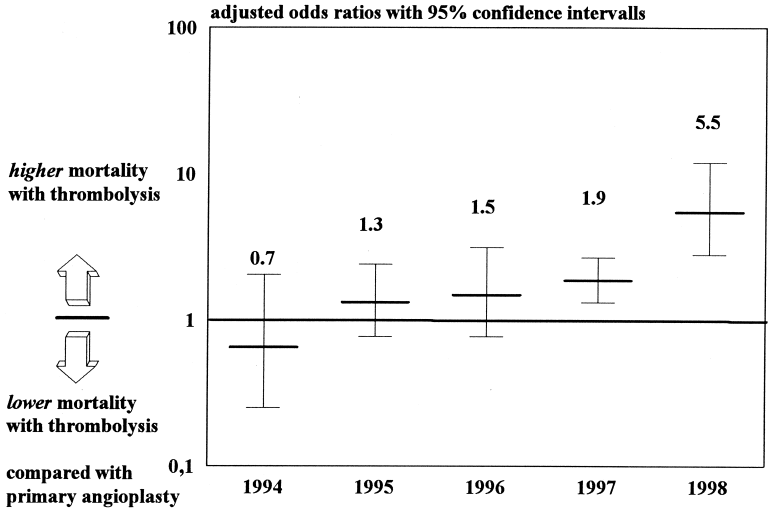

Figure 2. Multiple logistic regression analysis of hospital mortality comparing primary angioplasty with thrombolysis.

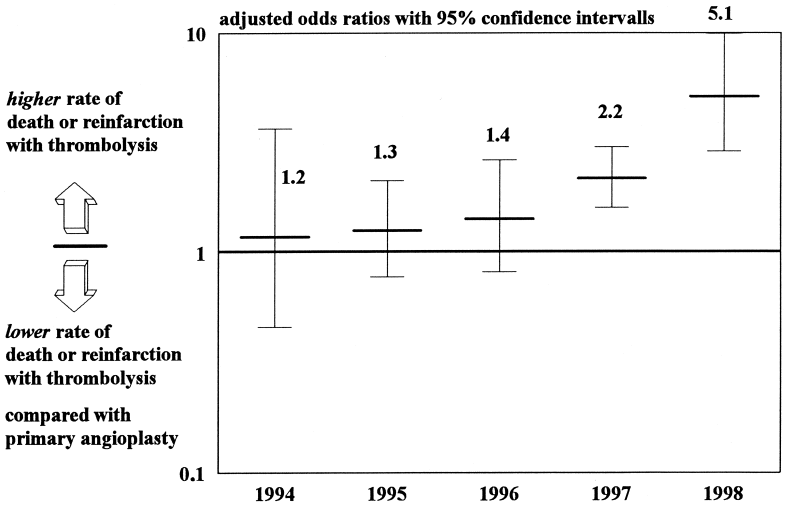

Figure 3. Multiple logistic regression analysis of the combined end point of death or reinfarction comparing primary angioplasty with thrombolysis.

outcome of primary angioplasty (12,13,40,41). Deficiencies of these factors at low volume hospitals for primary angioplasty have led to strict recommendations for performing primary angioplasty (35). Such differences between highly specialized hospitals and low volume hospitals have also been suggested to be the reason why registries (7–9) comparing primary angioplasty with thrombolysis in the "real world" failed to demonstrate a benefit of primary angioplasty as did randomized controlled trials (1–6,39).

Our data demonstrate a clear improvement in clinical outcome by treatment with primary angioplasty over the last years. One reason might be the growing experience of the treating physicians with primary angioplasty and improved clinical logistics. This hypothesis is supported by the records showing a decreasing proportion of patients with more than 90 min delay between admission to the hospital and the beginning of primary angioplasty. Berger et al. (41) and Cannon et al. (37) could show that shorter in-hospital delays are associated with a better clinical outcome. Another contributing factor could have been the recent introduction of stents (14–20) and IIb/IIIa receptor antagonists (21–23) in combination with primary angioplasty. However, the most recent data of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial (42), presented at the American Heart Association Scientific Meeting 1999 in Atlanta, Georgia, showed only a minor benefit of either adjunctive stenting or the use of abciximab in conjunction with primary angioplasty in AMI. The slightly higher use of beta-blockers and ACE inhibitors for patients treated with primary angioplasty compared with those treated with thrombolysis could have also contributed to the lower mortality. However, the proportion of patients being treated with these concomitant medications rose similarly in both treatment groups over the years.

We concluded that between 1994 and 1998 primary angioplasty for AMI was associated with a decreasing hospital mortality and reinfarction rate, whereas those events did not change in patients treated with thrombolysis. The most probable explanation for the improving outcome with primary angioplasty seems to be the growing experience of the physicians and the better hospital logistics.

Study limitations. This analysis of the MITRA and MIR data suffers from the limitations faced by all registries. Since MITRA and MIR are observational studies, it is not possible to control totally for the selection of patients to be treated with one of the two therapies. We did not collect information about the rate of technical success (Thrombolysis in AMI [TIMI] flow grade 3) of the angioplasty procedures or the use of stents and IIb/IIIa receptor inhibitors, so we were unable to control the results for these important variables. Therefore, it is not possible to draw definitive conclusions as to the mechanism responsible for the changing differences in short-term outcome between primary angioplasty and thrombolysis over the years. No hospital participated in both registries. Therefore, selection bias of the hospitals performing primary angioplasty could be present in the two registries. However, there was no apparent difference in the kind of angioplasty facilities in both registries (mainly community hospitals, only a few university hospitals). The trend of a decreasing mortality associated with primary angioplasty over the years was independently observed in the MITRA database and in the MIR database. Although we could analyze data from 1,385 patients treated with primary angioplasty, this number is much lower than the 8,733 patients who received intravenous thrombolysis. Therefore, other AMI registries should try to analyze their data accordingly in order to verify our results.

APPENDIX

The people and institutions who participated in the MITRA and MIR study are listed elsewhere (25,27).

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REFERENCES

1. O'Neill W, Timmis GC, Bourdillon PD, et al. A prospective randomized clinical trial of intracoronary streptokinase versus coronary angioplasty for acute myocardial infarction. N Engl J Med 1986;314:812–8.
2. Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheterization Laboratory Groups. N Engl J Med 1993;328:685–91.
3. Zijlstra F, de Boer MJ, Hoorntje JC, Reiffers S, Reiber JH, Suryapranata H. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680–4.
4. Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. N Engl J Med 1993;328:673–9.
5. Ribeiro EE, Silva LA, Carneiro R, et al. Randomized trial of direct coronary angioplasty versus intravenous streptokinase in acute myocardial infarction. J Am Coll Cardiol 1993;22:376–80.
6. 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 (published erratum appears in N Engl J Med 1997;24:287). N Engl J Med 1997;336:1621–8.
7. Every NR, Parsons LS, Hlatky M, Martin JS, Weaver WD. A comparison of thrombolytic therapy with primary coronary angioplasty for acute myocardial infarction. Myocardial Infarction Triage and Intervention Investigators. N Engl J Med 1996;335:1253–60.
8. Tiefenbrunn AJ, Chandra NC, French WJ, Gore JM, Rogers WJ. Clinical experience with primary percutaneous transluminal coronary angioplasty compared with alteplase (recombinant tissue-type plasminogen activator) for patients with acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMI- 2). J Am Coll Cardiol 1998;31:1240–5.
9. Danchin N, Vaur L, Genes N, et al. Treatment of acute myocardial infarction by primary coronary angioplasty or intravenous thrombolysis in the "Real World": 1-year results from a nationwide French survey. Circulation 1999;99:2639–44.
10. Zahn R, Schiele R, Gitt AK, et al. Primary angioplasty is superior to intravenous thrombolysis in all subgroups of patients: results from 9,906 patients with acute myocardial infarction. Circulation 1999;100 Suppl 1:359.
11. Grassman ED, Johnson SA, Krone RJ. Predictors of success and major complications for primary percutaneous transluminal coronary angioplasty in acute myocardial infarction. An analysis of the 1990 to 1994 Society for Cardiac Angiography and Interventions registries. J Am Coll Cardiol 1997;30:201–8.
12. Zahn R, Vogt A, Seidl K, et al. Balloon dilatation in acute myocardial infarct in routine clinical practice: results of the register of the Working Society of Leading Cardiologic Hospital Physicians in 4,625 patients. Z Kardiol 1997;86:712–21.
13. Christian TF, O'Keefe JH, DeWood MA, et al. Intercenter variability in outcome for patients treated with direct coronary angioplasty during acute myocardial infarction. Am Heart J 1998;135:310–7.
14. Ahmad T, Webb JG, Carere RR, Dodek A. Coronary stenting for acute myocardial infarction. Am J Cardiol 1995;76:77–80.
15. Rodriguez A, Bernardi V, Fernandez M, et al. In-hospital and late results of coronary stents versus conventional balloon angioplasty in acute myocardial infarction (GRAMI trial). Gianturco-Roubin in Acute Myocardial Infarction. Am J Cardiol 1998;81:1286–91.
16. Antoniucci D, Santoro GM, Bolognese L, Valenti R, Trapani M, Fazzini PF. A clinical trial comparing primary stenting of the infarct-related artery with optimal primary angioplasty for acute myocardial infarction: results from the Florence Randomized Elective Stenting in Acute Coronary Occlusions (FRESCO) trial. J Am Coll Cardiol 1998;31:1234–9.
17. Antoniucci D, Valenti R, Santoro GM, et al. Systematic direct angioplasty and stent-supported direct angioplasty therapy for cardiogenic shock complicating acute myocardial infarction: in-hospital and long-term survival. J Am Coll Cardiol 1998;31:294–300.
18. Neumann FJ, Walter H, Richardt G, Schmitt C, Schomig A. Coronary Palmaz-Schatz stent implantation in acute myocardial infarction. Heart 1996;75:121–6.
19. Suryapranata H, van't Hof AW, Hoorntje JC, de Boer MJ, Zijlstra F. Randomized comparison of coronary stenting with balloon angioplasty in selected patients with acute myocardial infarction. Circulation 1998;97:2502–5.
20. Stone GW, Brodie BR, Griffin JJ, et al. Clinical and angiographic follow-up after primary stenting in acute myocardial infarction: the primary angioplasty in myocardial infarction (PAMI) stent pilot trial. Circulation 1999;99:1548–54.
21. Azar RR, McKay RG, Thompson PD, et al. Abciximab in primary coronary angioplasty for acute myocardial infarction improves short- and medium-term outcomes. J Am Coll Cardiol 1998;32: 1996–2002.
22. Brener SJ, Barr LA, Burchenal JE, et al. Randomized, placebo-controlled trial of platelet glycoprotein IIb/IIIa blockade with primary angioplasty for acute myocardial infarction. ReoPro and Primary PTCA Organization and Randomized Trial (RAPPORT) Investigators. Circulation 1998;98:734–41.
23. van den Merkhof LF, Zijlstra F, Olsson H, et al. Abciximab in the treatment of acute myocardial infarction eligible for primary percutaneous transluminal coronary angioplasty. Results of the Glycoprotein Receptor Antagonist Patency Evaluation (GRAPE) pilot study. J Am Coll Cardiol 1999;33:1528–32.
24. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993;329:673–82.
25. Schuster S, Koch A, Burczyk U, Schiele R, et al. Early treatment of acute myocardial infarct: implementation of therapy guidelines in routine clinical practice, MITRA pilot phase. Z Kardiol 1997;86:273–83.
26. Zahn R, Schuster S, Schiele R, et al. Differences in patients with acute myocardial infarction treated with primary angioplasty or thrombolytic therapy. Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) Study Group. Clin Cardiol 1999;22:191–9.
27. Wagner S, Schneider S, Schiele R, et al. Acute myocardial infarction in Germany between 1996 and 1998: therapy and intrahospital course. Results of the myocardial infarction registry (MIR) in Germany. Z Kardiol 1999;88:857–67.
28. McGovern PG, Pankow JS, Shahar E, et al. Recent trends in acute coronary heart disease—mortality, morbidity, medical care and risk factors. The Minnesota Heart Survey Investigators. N Engl J Med 1996;334:884–90.
29. Goldberg RJ, Yarzebski J, Lessard D, Gore JM. A two decades (1975 to 1995) long experience in the incidence, in-hospital and long-term case-fatality rates of acute myocardial infarction: a communitywide perspective. J Am Coll Cardiol 1999;33:1533–9.
30. Goldberg RJ, Gorak EJ, Yarzebski J, et al. A communitywide perspective of sex differences and temporal trends in the incidence and survival rates after acute myocardial infarction and out-of-hospital deaths caused by coronary heart disease. Circulation 1993;87:1947–53.
31. Goldberg RJ, Gore JM, Alpert JS, Dalen JE. Incidence and case fatality rates of acute myocardial infarction (1975–1984): the Worcester Heart Attack study. Am Heart J 1988;115:761–7.
32. Gil M, Marrugat J, Sala J, et al. Relationship of therapeutic improvements and 28-day case fatality in patients hospitalized with acute myocardial infarction between 1978 and 1993 in the REGICOR study, Gerona, Spain. The REGICOR Investigators. Circulation 1999;99:1767–73.
33. Jollis JG, DeLong ER, Peterson ED, et al. Outcome of acute myocardial infarction according to the specialty of the admitting physician. N Engl J Med 1996;335:1880–7.
34. Chen J, Radford MJ, Wang Y, Marciniak TA, Krumholz HM. Do "America's Best Hospitals" perform better for acute myocardial infarction? N Engl J Med 1999;340:286–92.
35. Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction: executive summary and recommendations: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). Circulation 1999;100:1016–30.
36. 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 randomized trials of more than 1,000 patients (published erratum appears in Lancet 1994;343:742). Lancet 1994;343:311–22.
37. Cannon CP, Gibson M, Lambrew CT, et al. Relationship of time to treatment and door-to-balloon time to mortality in 27,080 patients with acute myocardial infarction treated with primary angioplasty. Circulation 1999;100 Suppl 1:360.
38. Zahn R, Schiele R, Hauptmann KE, et al. Longer prehospital delays are associated with increasing mortality in patients with acute myocardial infarction treated with intravenous thrombolysis but not in patients treated with primary angioplasty. Circulation 1999;100 Suppl 1:359.
39. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review (published erratum appears in J Am Med Assoc 1998;279:1876). J Am Med Assoc 1997;278: 2093–8.
40. Caputo RP, Ho KK, Stoler RC, et al. Effect of continuous quality improvement analysis on the delivery of primary percutaneous transluminal coronary angioplasty for acute myocardial infarction. Am J Cardiol 1997;79:1159–64.
41. Berger PB, Ellis SG, Holmes DRJ, et al. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in Acute Coronary Syndromes (GUSTO-IIb) trial. Circulation 1999;100:14–20.
42. Stone GW. Stenting and IIb/IIIa receptor blockade in acute myocardial infarction: an introduction to the CADILLAC trial. J Invasive Cardiol 1999;10 Suppl B:36B–47B.