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# A COMPARISON OF THROMBOLYTIC THERAPY WITH PRIMARY CORONARY ANGIOPLASTY FOR ACUTE MYOCARDIAL INFARCTION

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## ABSTRACT

***Background*** Several relatively small randomized trials have shown that primary angioplasty results in a better short-term outcome than thrombolytic therapy in patients with acute myocardial infarction. These results, however, have not been duplicated other than in investigational trials.

***Methods*** We compared mortality during hospitalization and long-term mortality, as well as the use of resources, among 1050 patients in a primary-angioplasty group and 2095 patients in a thrombolytic-therapy group. Patients were selected from the Myocardial Infarction Triage and Intervention Project Registry cohort of 12,331 consecutive patients admitted with acute myocardial infarction to 19 Seattle hospitals between 1988 and 1994. Because of the potential for selection bias, several subgroup analyses were performed that included patients eligible for thrombolysis, high-risk patients, and patients in the primary-angioplasty group who were treated at hospitals with high volumes of angioplasty.

***Results*** There was no significant difference in mortality during hospitalization or long-term follow-up between patients in the thrombolytic-therapy group and those in the primary-angioplasty group (mortality during hospitalization, 5.6 percent and 5.5 percent, respectively; $P = 0.93$; adjusted hazard ratio for the risk of death within three years after primary angioplasty, 0.95; 95 percent confidence interval, 0.8 to 1.2). There was also no significant difference in mortality between high-risk subgroups of patients in the two treatment groups. The rates of procedures and costs were lower among patients in the thrombolytic-therapy group both at the time of hospital discharge and after three years of follow-up (30 percent fewer coronary angiograms, 15 percent fewer coronary angioplasties, and 13 percent lower costs after three years of follow-up).

***Conclusions*** In a community setting, we observed no benefit in terms of either mortality or the use of resources with a strategy of primary angioplasty rather than thrombolytic therapy in a large cohort of patients with acute myocardial infarction. (N Engl J Med 1996;335:1253-60.)



SEVERAL randomized, controlled trials have shown that the short-term outcome in patients with acute myocardial infarction is better after primary angioplasty than after thrombolytic therapy.[1-3] In a recent pooled analysis of all trials of primary angioplasty, there was a 44 percent reduction in mortality during hospitalization (odds ratio, 0.56; 95 percent confidence interval, 0.53 to 0.94) and a 9 percent reduction in mortality at one year (hazard ratio, 0.91; 95 percent confidence interval, 0.42 to 2.00).[4]

Due to the small size of each of the trials, the real magnitude of any beneficial effect of primary angioplasty — especially beyond 30 days — is unclear. In addition, few data have been reported on the long-term use of resources associated with either reperfusion strategy. Whether these results can be duplicated in larger series or outside centers performing a high volume of primary angioplasty has not been evaluated.

In the absence of larger randomized trials, carefully designed cohort studies can be used to supplement our knowledge about these treatments. The Myocardial Infarction Triage and Intervention (MITI) Project Registry includes detailed data on a cohort of 12,331 consecutive patients with acute myocardial infarction in Seattle. The registry data can be used to compare the short- and long-term outcome in patients treated with either primary angioplasty or thrombolytic therapy. Although this is not a randomized comparison, the choice of reperfusion strategy was often a result of which hospital the patient

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was admitted to. That is, patients admitted to one of three hospitals that favor primary angioplasty were likely to receive this treatment, and patients admitted to other Seattle hospitals were usually treated with thrombolytic therapy. Thus, the treatments can be compared with limited selection bias.

## METHODS

### Patients

The subjects of this study were selected from a population of 12,331 patients with acute myocardial infarction who were enrolled in the MITI registry between 1988 and 1994. Characteristics of the registry, data-gathering procedures, and reliability have been described previously.[5] Briefly, the MITI Project is a collaborative effort to evaluate new treatment strategies for patients with acute myocardial infarction and also includes a registry of all patients admitted for suspected myocardial infarction in the Seattle metropolitan area. For patients transferred to a different institution during the index hospitalization, medical records were abstracted at the second hospital so that each patient had a continuous record of care. The study was approved by the University of Washington Human Subjects Review Committee.

The primary-angioplasty cohort was defined as patients with myocardial infarction, not treated with thrombolytic therapy, who underwent diagnostic angiography within six hours after admission to the hospital and then immediately underwent percutaneous transluminal coronary angioplasty or coronary-artery bypass surgery, or did not receive reperfusion therapy. The thrombolytic-therapy cohort was defined as patients with myocardial infarction treated with thrombolytic therapy within six hours after admission. Thrombolytic therapy was given at the treating physician's discretion according to standard protocols with alteplase (65 percent), streptokinase (32 percent), or prourokinase (3 percent). A small proportion of patients in this group were treated before hospitalization (8 percent).

Hospitals participating in the MITI registry include 2 university hospitals, 2 hospitals affiliated with staff-model health maintenance organizations, 1 Veterans Affairs hospital, and 14 community hospitals. During most of the study period, 11 (58 percent) of the participating hospitals had on-site catheterization laboratories, and 6 (32 percent) performed bypass surgery. Primary angioplasty was performed in at least 40 percent of all patients with acute infarction who received short-term reperfusion treatment in three of the participating hospitals.

### Data Collection

Trained abstractors collected detailed data on the patients' demographic characteristics, prehospital treatment, clinical presentation, and hospital course and on procedures performed from the patients' records within three months after discharge or death. Deaths that occurred after discharge, readmissions, and the rates of subsequent use of procedures were obtained by linking the MITI registry to the Washington State Comprehensive Hospital Abstract Reporting system. This data base includes information on the use of resources, hospital charges, and vital status for every hospital admission in the state of Washington. The rates of readmission (with a diagnosis of primary cardiac disease according to the *International Classification of Diseases, 9th Revision, Clinical Modification*) and use of cardiac procedures were calculated one and three years after discharge and are cumulative. The rates of use of procedures after discharge did not include procedures performed during the index admission. All charges were converted to 1995 dollars, and costs were calculated by multiplying charges by the Medicare cost-to-charge ratio for each participating hospital. To adjust for outliers in the cost comparison, the top and bottom 1 percent of charges were deleted from the analysis.

### Statistical Analysis

We used the chi-square test and Student's t-test to test for significant differences in base-line characteristics between patients who underwent primary angioplasty and those treated with thrombolytic therapy. Lengths of hospital stay and costs were compared by the Mann–Whitney nonparametric test. The rates of procedure use after discharge and the rates of readmission to the hospital were compared at one and three years, and long-term mortality was compared with Kaplan–Meier plots and the log-rank test. To test whether there was an association between the use of primary angioplasty and long-term mortality independent of base-line differences, we constructed a series of Cox regression models. For each comparison, the models were evaluated with and without the complications of stroke and recurrent infarction, since these factors may have been associated with both the treatment and outcome. In all models, thrombolytic therapy was considered the standard of comparison.

To limit possible selection bias, several subgroup analyses were performed. The first subgroup analysis included only patients who were eligible to receive thrombolysis: those presenting with ST-segment elevation and a systolic blood pressure of less than 180 mm Hg and without evidence of shock on admission, a history of bypass surgery, or a history of stroke or bleeding (gastrointestinal or other sites). In a second subgroup analysis, we compared the outcome in patients treated with thrombolytic therapy with that in patients in the primary-angioplasty group who were admitted to one of the three hospitals in which primary angioplasty was performed in at least 40 percent of all cases of reperfusion. All patients in this subgroup were also eligible to undergo thrombolysis. In this comparison, we assumed that primary angioplasty was performed because of the physician's preference for this form of reperfusion and not because of specific characteristics of the patients. The final subgroup analysis included only patients classified as high risk as defined in the Primary Angioplasty in Myocardial Infarction (PAMI)[2] trial: those with an anterior location of infarct, age greater than 70 years, or heart rate greater than 100 beats per minute.

## RESULTS

### Base-Line Characteristics

From a cohort of 12,331 patients with acute infarction who were enrolled in the MITI registry, we studied 1272 patients in the primary-angioplasty group and 2664 patients in the thrombolytic-therapy group. Electrocardiographic data were missing for 156 patients in the primary-angioplasty group and 569 patients in the thrombolytic-therapy group. These patients were excluded from the analysis. An additional 66 patients in the primary-angioplasty group who were treated for ST-segment elevation between 6 and 24 hours after admission were also excluded from the analysis. We therefore studied a total of 1050 patients in the primary-angioplasty group and 2095 patients in the thrombolytic-therapy group. There was no difference in the mortality rates during hospitalization between these excluded patients and those included in the primary-angioplasty cohort.

The base-line characteristics of the thrombolytic-therapy and primary-angioplasty cohorts were similar. There were no significant differences in age, sex, race, or the proportion of patients with prior myocardial infarction or heart failure (Table 1). The thrombolytic-therapy cohort had a lower proportion of patients

**TABLE 1.** BASE-LINE CHARACTERISTICS OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION ACCORDING TO TREATMENT GROUP.*

| CHARACTERISTIC | THROMBOLYTIC THERAPY (N=2095) | PRIMARY ANGIOPLASTY (N=1050) | P VALUE |
|---|---|---|---|
| Age (yr) | 59.8±11.9 | 59.9±11.9 | 0.89 |
| Female sex (%) | 23.9 | 23.4 | 0.76 |
| Prior infarct (%) | 13.0 | 14.8 | 0.16 |
| Prior heart failure (%) | 3.7 | 3.3 | 0.62 |
| Prior bypass surgery (%) | 5.5 | 7.8 | 0.01 |
| History of stroke (%) | 4.2 | 6.5 | 0.16 |
| History of gastrointestinal bleeding (%) | 0.8 | 2.8 | 0.007 |
| Systolic blood pressure >180 mm Hg (%) | 5.9 | 7.8 | 0.1 |
| Heart rate >100 beats/min (%) | 10.0 | 11.6 | 0.19 |
| Systolic blood pressure <100 mm Hg (%) | 10.3 | 11.7 | 0.32 |
| Anterior location of infarct (%) | 37.3 | 34.2 | 0.08 |
| High risk (%)† | 54.6 | 57.0 | 0.28 |
| Time to treatment (hr) | 1.0±1.0 | 1.7±1.2 | <0.001 |

*Plus–minus values are means ±SD.

†High risk was defined according to the criteria of the PAMI trial.[2]

who were potentially ineligible for thrombolysis because of a history of bypass surgery (5.5 percent vs. 7.8 percent, P=0.01), stroke (4.2 percent vs. 6.5 percent, P=0.16), or gastrointestinal bleeding (0.8 percent vs. 2.8 percent, P=0.007) or a systolic blood pressure of more than 180 mm Hg on admission (5.9 percent vs. 7.8 percent, P=0.1). There were no significant differences in heart rate, blood pressure, or the proportion of patients classified as high risk according to the PAMI criteria at admission.

Patients in the thrombolytic-therapy group were treated sooner than were those in the primary-angioplasty group (mean [±SD] interval from arrival at the emergency room to thrombolytic therapy, 1.0±1.0 hour, as compared with a mean interval from arrival at the emergency room to balloon inflation of 1.7±1.2 hours; P<0.001). The 25th, 50th, and 75th percentile values for the time to treatment were 0.47, 0.78, and 1.28 hours, respectively, in the thrombolytic-therapy group and 0.87, 1.32, and 2.18 hours in the primary-angioplasty group.

Ten of the 19 participating hospitals performed at least one primary angioplasty procedure. Hospitals with higher volumes of primary angioplasty treated patients more promptly than those with lower volumes (time to treatment, 1.5 vs. 2.3 hours, P<0.001), but there was no association between volume and the proportion of successful angioplasty procedures (Table 2). Although hospitals with low volumes of primary angioplasty had higher rates of mortality during hospitalization in a univariate comparison (8.1 percent, as compared with 4.5 percent for the high-volume hospitals; P<0.01), this difference was no longer significant after multivariate adjustment.

### Outcome during Hospitalization

By definition, all patients in the primary-angioplasty group underwent coronary angiography. Of those who underwent immediate angiography, 93 percent underwent primary angioplasty, 3 percent underwent immediate coronary-artery bypass surgery (<6 hours after admission), and in 4 percent there was no attempt at reperfusion. The overall success rate for angioplasty was 89 percent as reported by the operating physicians and improved during later years of the registry (87 percent in 1988 to 1991 vs. 90 percent in 1992 to 1994, P=0.003).

Patients treated with thrombolytic therapy also had high rates of use of procedures (74 percent underwent angiography, and 32 percent underwent coronary angioplasty) (Fig. 1). Of the patients treated with thrombolytic therapy who underwent angiography, 697 underwent angiography on the day of admission (351 for recurrent chest pain), 537 of whom also underwent revascularization on the day of admission.

There was no significant difference in the proportions of patients who underwent coronary-artery bypass surgery. Patients treated with thrombolytic therapy were more likely to have a stroke during hospitalization (1.5 percent vs. 0.7 percent, P=0.04), but there was no significant difference in

**TABLE 2.** CHARACTERISTICS OF THE HOSPITALS AND PATIENT OUTCOME ACCORDING TO THE VOLUME OF PRIMARY ANGIOPLASTIES PERFORMED.*

| CHARACTERISTIC | LOW-VOLUME HOSPITAL (N=7) | HIGH-VOLUME HOSPITAL (N=3) |
|---|---|---|
| Mean no. of elective and emergency coronary interventions performed in 1995 (range) | 301 (43–600) | 262 (114–422) |
| Total no. of cases of emergency reperfusion of infarction in MITI registry (primary angioplasty or thrombolytic therapy) | 1394 | 995 |
| No. of patients treated with primary angioplasty for reperfusion (%) | 207 (15) | 801 (80) |
| Success rate for angioplasty — % | 86 | 89 |
| Time to treatment — hr† | 2.3 | 1.5 |
| In-hospital mortality — %‡ | 8.1 | 4.5 |

*A low-volume hospital was one that performed primary angioplasty in <40 percent of patients treated with reperfusion, and a high-volume hospital was one that performed primary angioplasty in ≥40 percent of such patients.

†P<0.001 for the comparison between groups.

‡P<0.01 for the comparison between groups.

the proportion of patients with reinfarction (4.3 percent vs. 3.5 percent, P = 0.37). Patients in the thrombolytic-therapy group were hospitalized a mean of 1.1 days longer than patients in the primary-angioplasty group (7.9±5.3 vs. 6.8±4.4 days; median, 7 vs. 6 days; P<0.001), but their mean total hospital costs were lower ($16,838±12,480 vs. $19,702±12,175; median, $12,600 vs. $16,300; P<0.001). There was no significant difference in the mortality rate during hospitalization between the cohorts (5.6 percent vs. 5.5 percent, P = 0.93).

#### Long-Term Outcome

Patients in the thrombolytic-therapy group underwent fewer coronary procedures after discharge than those in the primary-angioplasty group. Patients treated with thrombolytic therapy were less likely to have undergone coronary angiography after discharge at either one year (7.4 percent vs. 13.2 percent, P<0.001) or three years (19.7 percent vs. 28.3 percent, a 30 percent reduction; P<0.001) (Fig. 2). Patients treated with thrombolytic therapy were also significantly less likely to have undergone coronary angioplasty after discharge at one year (6.6 percent vs. 9.0 percent, P = 0.03) but not at three years (15.9 percent vs. 18.8 percent, a 15 percent reduction; P = 0.15). There were no significant differences between the two groups in the proportions of patients who had undergone bypass surgery or had been admitted to the hospital at one or three years of follow-up. The mean total cumulative inpatient costs were 13 percent lower at three years in patients treated with thrombolytic therapy ($22,163±18,118 vs. $25,459±17,543; median, $16,500 vs. $19,600; P<0.001).

In an unadjusted comparison, there was no significant difference in long-term survival between groups (Fig. 3). In order to evaluate the association between the reperfusion strategy and long-term mortality independently of differences in base-line characteristics, a series of Cox regression analyses were performed. Factors that independently predicted a higher risk of death within three years included a heart rate of more than 100 beats per minute on admission, a history of heart failure, a history of bypass surgery, older age, prior myocardial infarction, and an anterior location of the infarct (Fig. 4). After adjustment for these factors, there was no association between the use of primary angioplasty and long-term mortality (hazard ratio, 0.95; 95 percent confidence interval, 0.8 to 1.2). When complications of myocardial infarction such as stroke and reinfarction were added to the model, there was still no association between the use of primary angioplasty and lower long-term mortality (hazard ratio, 0.94; 95 percent confidence interval, 0.8 to 1.2).

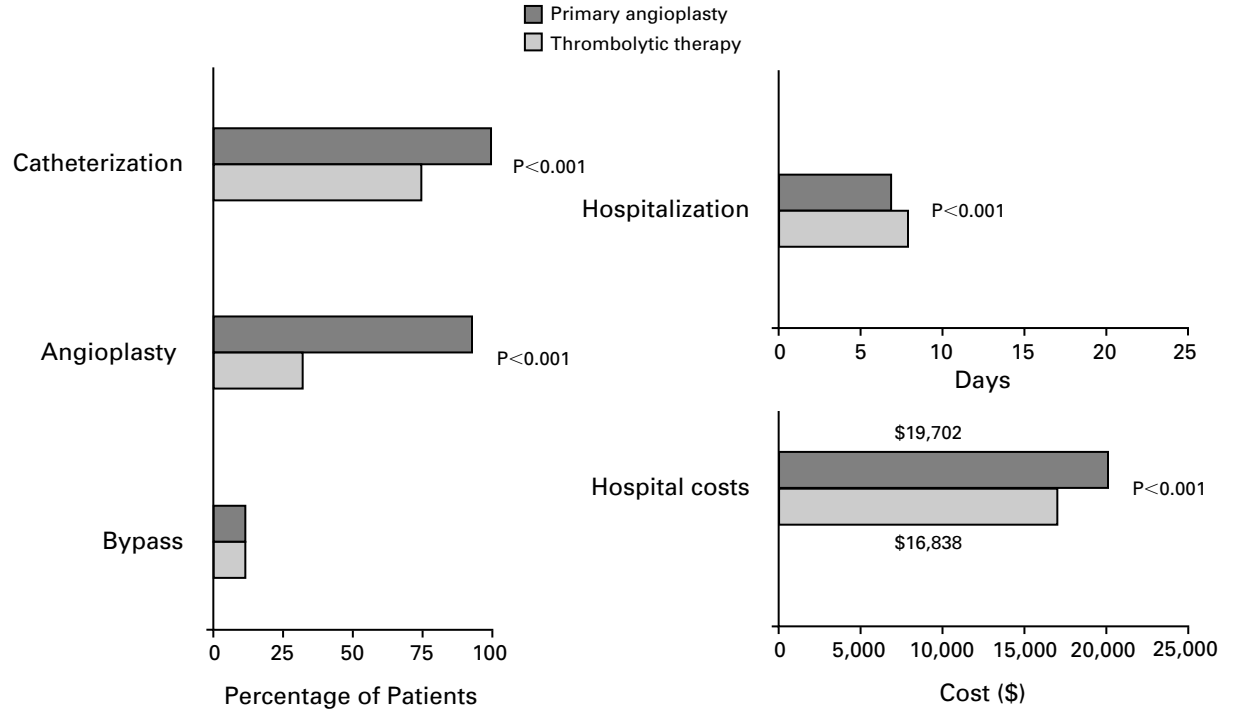


**Figure 1.** Use of Resources during Index Hospitalization for Acute Myocardial Infarction in 1050 Patients in the Primary-Angioplasty Group and 2095 Patients in the Thrombolytic-Therapy Group.

**Subgroup Analyses**

Because there may have been some selection bias in the physicians' choice of reperfusion strategies, we performed a series of subgroup analyses. In the first subgroup analysis, we included only patients who were eligible for thrombolytic therapy according to our criteria (1674 in the thrombolytic-therapy group and 702 in the primary-angioplasty group). Except for a longer time to treatment in the patients treated with primary angioplasty (0.9±0.8 vs. 1.5±1.1 hours, $P<0.001$), there were no significant differences in demographic or base-line clinical characteristics between the groups. The mortality rate during hospitalization was nearly identical (4.4 percent in the thrombolytic-therapy group and 4.6 percent in the primary-angioplasty group, $P=0.89$). During long-term follow-up, patients in the thrombolytic-therapy group were significantly less likely to undergo coronary angiography after discharge than those in the primary-angioplasty group (Fig. 5). There was no significant difference in the rate of bypass surgery or coronary angioplasty after discharge or in the proportion of patients with at least one hospital readmission. Total hospital costs, including the index admission, were lower in the thrombolytic-therapy cohort ($21,760±17,438 vs. $23,882±15,768; $P=0.003$). There was no significant difference in the unadjusted long-term mortality rate (12.0 percent vs. 13.6 percent at three years, $P=0.79$) or the adjusted long-term mortality rate (hazard ratio, 1.0; 95 percent confidence interval, 0.74 to 1.4).

We performed a second subgroup analysis in which the primary-angioplasty cohort included only patients admitted to the three hospitals that performed primary angioplasty in at least 40 percent of patients treated with reperfusion (1674 in the thrombolytic-therapy group and 438 in the primary-angioplasty group). There were no substantial differences in base-line characteristics between cohorts. After three years of follow-up, patients in the thrombolytic-therapy group were less likely than patients in the primary-angioplasty group to have had at least one coronary angiogram after discharge (19 percent vs. 29 percent, $P=0.001$), but there were no significant differences in the rates of coronary angioplasty, bypass surgery, or hospital readmission. There was no significant difference in the mortality rate during hospitalization (5.2 percent vs. 5.4 percent, respectively; $P=0.87$) or the long-term mortality rate (12.1 percent vs. 13.3 percent at three years, $P=0.76$) between cohorts. There was also no significant difference in the adjusted long-term mortality rate (hazard ratio, 1.0; 95 percent confidence interval, 0.51 to 2.0).

Finally, a subgroup analysis was performed comparing the outcome only in patients classified as high risk according to the criteria of the PAMI trial. In this comparison, there was no significant differ-

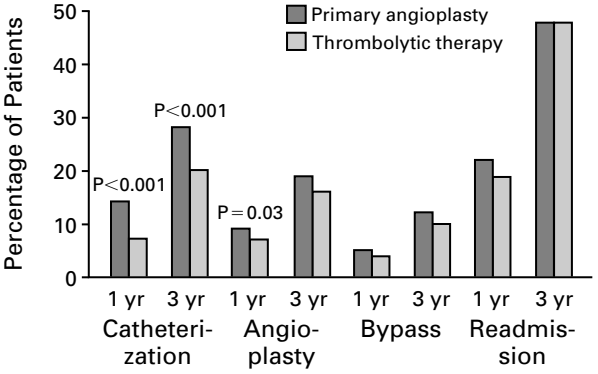


**Figure 2.** Use of Resources after the Initial Hospitalization by 1050 Patients in the Primary-Angioplasty Group and 2095 Patients in the Thrombolytic-Therapy Group.

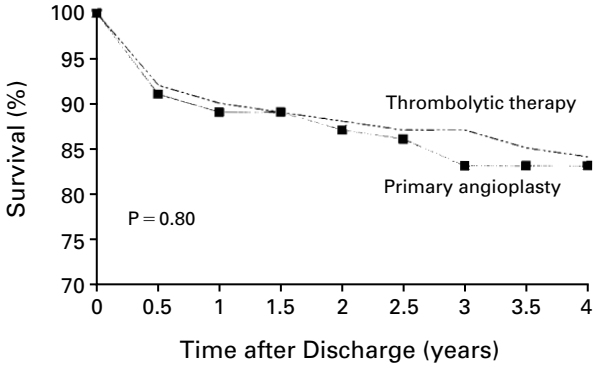


**Figure 3.** Cumulative Survival among 1050 Patients in the Primary-Angioplasty Group and 2095 Patients in the Thrombolytic-Therapy Group.

There was no significant difference in unadjusted long-term survival between cohorts.

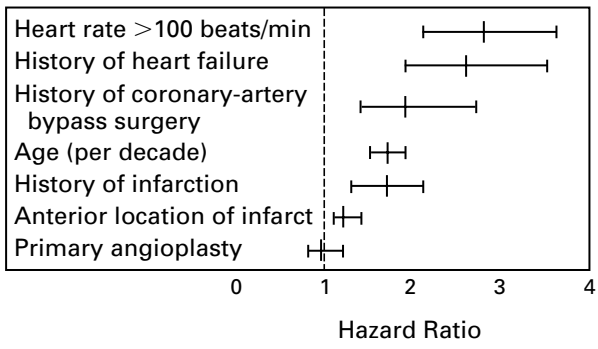


**Figure 4.** Factors Analyzed for an Association with a Higher Risk of Death at Three Years in 1050 Patients in the Primary-Angioplasty Group and 2095 Patients in the Thrombolytic-Therapy Group.

Hazard ratios to the right of the dotted line are associated with a higher risk of long-term mortality. After adjustment for all measured factors that predict mortality, there was no association between the use of primary angioplasty and long-term mortality (adjusted hazard ratio, 0.95; 95 percent confidence interval, 0.8 to 1.2).

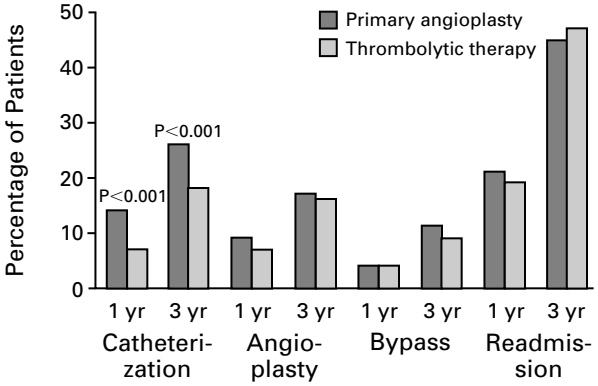


**Figure 5.** Use of Resources after the Initial Hospitalization by a Subgroup of 702 Patients in the Primary-Angioplasty Group and 1674 Patients in the Thrombolytic-Therapy Group Who Were Eligible for Thrombolysis.

ence in the mortality rate during hospitalization (8.1 percent in the thrombolytic-therapy group vs. 8.7 percent in the primary-angioplasty group, $P = 0.70$) or the long-term mortality rate (17.8 percent vs. 24.8 percent at three years of follow-up, $P = 0.48$). There was no significant difference in the long-term mortality rate after multivariate adjustment for differences in base-line characteristics (hazard ratio, 1.1; 95 percent confidence interval, 0.82 to 1.53).

## DISCUSSION

Since the first trials of thrombolytic therapy for the treatment of acute myocardial infarction, investigators have speculated that rapid reperfusion of a completely occluded coronary artery would improve the outcome. The use of primary angioplasty has been suggested to extend or enhance this benefit because arteries can be opened more reliably with angioplasty than with thrombolytic therapy.[6,7] Randomized, controlled trials comparing primary angioplasty with thrombolytic therapy have, on the whole, shown improved short-term outcome in patients treated with primary angioplasty (Table 3).[1-3] However, these studies lack data on the long-term outcome, and the results have not been confirmed in larger multicenter trials.

In the present study, we used observational data on over 3000 patients with acute myocardial infarction to evaluate whether the results of these randomized trials could be replicated in a community setting. Although the patients were not randomly assigned to treatment, there were no substantial differences in base-line demographic or clinical characteristics between patients in the thrombolytic-therapy group and those in the primary-angioplasty group. There was no difference in the mortality rate during hospitalization or in the long-term mortality rate between the two cohorts. Subgroup analyses of patients with no contraindications to thrombolytic therapy, patients admitted to centers with higher volumes of primary angioplasty, and high-risk patients each showed similar rates of mortality during hospitalization and long-term follow-up in the two treatment groups.

The equivalent mortality rates for thrombolysis and angioplasty observed in our study contrast with the improved outcome during hospitalization observed in patients treated with primary angioplasty in the two largest published randomized trials. Grines et al. found a significantly lower composite end point of reinfarction or death in 195 patients randomly assigned to primary angioplasty both at hospital discharge and after six months of follow-up.[2] Similarly, Zijlstra and coworkers found lower rates of death during hospitalization and of recurrent myocardial infarction in 149 patients randomly assigned to primary angioplasty.[3,8] However, two other randomized trials found no improvement in the outcome during hospitalization.[9,10] Limited long-term follow-up data from the randomized trials of primary angioplasty have indicated that the benefit of primary angioplasty is sustained.[2,8]

How then do we explain the disparate findings between our study and those of randomized trials? First, the mortality rate during hospitalization among patients treated with thrombolytic therapy in our study was somewhat lower than that reported in the larger randomized trials. A possible reason for this observation is a lower rate of stroke in our study (1.5 percent) than in the PAMI trial (3.5 percent). Although the stroke rate in the MITI registry is consistent with that in other trials of thrombolytic therapy,[11,12] strokes in the registry were ascertained by reviewing the medical records and may not be as accurately classified as those in randomized trials. Another factor that may have contributed to the lower observed mortality rate among patients treated with thrombolytic therapy was the high rate of angiography and revascularization on the day of hospital admission. It is likely that the majority of these procedures were performed because thrombolysis failed, and this aggressive use of early mechanical revascularization in patients treated with thrombolytic therapy may have resulted in a lower rate of mortality during hospitalization. Finally, the lower mortality rate among patients treated with thrombolytic therapy may be associated with the fact that treatment was earlier than in the PAMI trial (time to treatment, 198 vs. 230 minutes).

In addition to the lower mortality rate among the patients treated with thrombolytic therapy, we observed a higher mortality rate during hospitalization in the primary-angioplasty cohort than that reported in the randomized trials. Primary angioplasty requires greater technical expertise than the delivery of thrombolytic therapy. It is unknown whether community hospitals can perform primary angioplasty as

**TABLE 3.** CHARACTERISTICS OF THE PATIENTS AND OUTCOME DURING HOSPITALIZATION IN RANDOMIZED, CONTROLLED TRIALS COMPARING PRIMARY ANGIOPLASTY WITH THROMBOLYTIC THERAPY.*

| VARIABLE | GRINES ET AL.[2] | ZIJLSTRA ET AL.[3] | GIBBONS ET AL.[9] | RIBEIRO ET AL.[10] |
|---|---|---|---|---|
| No. of patients randomized | 395 | 301 | 108 | 100 |
| Years of study | 1990–1992 | 1990–1993 | 1989–1991 | 1989 |
| Criteria for exclusion from study | Shock, left bundle-branch block | Age >75 yr | Shock | Age >75 yr, prior CABG |
| Thrombolytic agent | t-PA | Streptokinase | t-PA | Streptokinase |
| Time from randomization to treatment (min) | PTCA, 60; TT, 30 | PTCA, 61; TT, 30 | Not reported | PTCA, 238; TT, 179 |
| Patients who received TT who also underwent angiography/PTCA (%) | 63/36 | 100 (routine at 3 mo)/31 | Not reported/36 | 100 (routine at 48 hr)/48 |
| Mortality during hospitalization (%) | PTCA, 2.6; TT, 6.5 | PTCA, 2.0; TT, 7.0 | PTCA, 2.0; TT, 0.0 | PTCA, 6.0; TT, 2.0 |
| Reinfarction (%) | PTCA, 2.6; TT, 6.5 | PTCA, 1.0; TT, 10.0 | PTCA, 0.0; TT, 4.0 | Not reported |

*CABG denotes coronary-artery bypass grafting, PTCA percutaneous transluminal coronary angioplasty, t-PA tissue plasminogen activator, and TT thrombolytic therapy.

quickly and as effectively as the high-volume expert centers in the randomized trials. Indeed, the angioplasty success rate in our study (89 percent) was substantially lower than that reported by the PAMI investigators (98 percent). Although this may have been associated with the earlier initiation of the registry we used (1988), it is also possible that the performance of primary angioplasty in this community setting may not be equal to that in high-volume and specialized centers. In MITI-registry hospitals, higher-volume hospitals had earlier treatment times and lower unadjusted rates of mortality during hospitalization than the lower-volume hospitals. On the other hand, a subgroup analysis limited to higher-volume hospitals did not show that the outcome of primary angioplasty was better in those hospitals. Thus, it is unlikely that the volume of procedures performed explains the somewhat higher mortality rate observed among the patients in the primary-angioplasty group. Another explanation could be that certain angioplasty methods employed by expert centers in the randomized trials, such as the aggressive use of heparin (activated clotting time, >350 seconds)[13] and avoidance of non-ionic contrast medium,[14] were not routinely used by MITI-registry hospitals.

Other differences between the present study and reported randomized trials could not be addressed and are limitations of this analysis. First, although the three-year mortality rate for patients in the primary-angioplasty group is similar to those of other registries of primary angioplasty,[15,16] there was insufficient power to detect a small difference (<20 percent) in long-term mortality. Second, limitations in data collection required the exclusion of a small number of patients who underwent primary angioplasty 6 to 24 hours after admission. Since the mean time from the onset of chest pain to presentation in our cohort was 3.0 hours, it is unlikely that the inclusion of patients treated 9 hours after the onset of pain would have substantially altered our results.

Finally, the design strengths of the randomized controlled trial cannot be underestimated. Although we were able to adjust for any differences in measured base-line characteristics between the cohorts, we could not adjust for unmeasured differences that may have influenced both the choice of reperfusion strategy and the outcome.

One potential advantage of primary angioplasty is the possibility of reducing the rates of readmission and subsequent revascularization procedures by performing these procedures during the index hospitalization. Although we expected patients treated with thrombolytic therapy to undergo more procedures after discharge than those treated initially with primary angioplasty, we found just the opposite.

The higher rate of subsequent procedures among patients in the primary-angioplasty group may be a result of the use of a more invasive strategy by physicians who prefer primary angioplasty. In addition, since most patients in the primary-angioplasty group underwent coronary angioplasty during the index admission (as compared with 32 percent of those treated with thrombolytic therapy), the chance of clinical restenosis and repeated cardiac procedures is probably greater in the primary-angioplasty cohort.

Other studies with at least one year of follow-up after primary angioplasty have shown both higher[9] and lower[17] rates of subsequent procedures among patients randomly assigned to angioplasty. These discordant findings are most likely due to differences in physicians' practice styles as well as a higher rate of use of invasive cardiac procedures in American[9] than in European[17] hospitals. From our analysis, however, it appears that there could be substantial nationwide cost savings if the $3,000 savings per pa-

tient treated with thrombolytic therapy were applied to the nearly 200,000 patients who are eligible for thrombolysis each year.

In this community sample of patients treated with thrombolytic therapy or primary angioplasty there was no difference between groups in short- or long-term mortality. The rate of subsequent procedures and cumulative costs tended to be higher in the primary-angioplasty group. In all likelihood these findings reflect the effectiveness of these therapies in uncontrolled settings in hospitals with relatively low volumes of use of these procedures.

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