Patient Outcomes After Fibrinolytic Therapy for Acute Myocardial Infarction at Hospitals With and Without Coronary Revascularization Capability

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OBJECTIVES
This study evaluated clinical outcomes in patients with acute myocardial infarction (MI) treated with fibrinolytic therapy in hospitals with and without coronary revascularization capability.

BACKGROUND
Patients with MI may have better outcomes when admitted to certain hospitals with coronary revascularization capability. Development of regional heart care centers for the treatment of MI has been proposed.

METHODS
We performed a retrospective analysis of 25,515 U.S. patients enrolled in the Global Use of Streptokinase and TPA (alteplase) for Occluded Coronary arteries (GUSTO-I) trial. Outcomes of patients admitted to hospitals with and without coronary revascularization capability were analyzed. We also analyzed patients who remained in hospitals without coronary revascularization capability compared with those transferred to hospitals with revascularization capability.

RESULTS
Baseline characteristics and complications were similar between patients in the two hospital types. Patients in hospitals with coronary revascularization capability more often underwent cardiac catheterization (78.1% vs. 59.2%; p < 0.001), angioplasty (34.6% vs. 22.6%; p < 0.001), or bypass surgery (14.1% vs. 10.4%; p < 0.001) but had a similar adjusted 30-day (odds ratio [OR] 0.91, 95% confidence interval [CI] 0.82 to 1.02) and one-year (OR 0.98, 95% CI 0.90 to 1.07) mortality. Forty percent of patients admitted to hospitals without revascularization capability were transferred, with 94% of transfer patients undergoing angiography. Almost 80% of transfers occurred >48 h after hospital admission.

CONCLUSIONS
Patients receiving fibrinolytic therapy for acute MI admitted to hospitals without coronary revascularization capability appear to have outcomes similar to those of patients admitted to hospitals with such capability when aspirin and beta-adrenergic blocking agents are given appropriately and transfer is available for angiography and angioplasty as needed. (J Am Coll Cardiol 2002;40:1034–40) © 2002 by the American College of Cardiology Foundation

Most patients with acute myocardial infarction (MI) are treated in community hospitals without coronary revascularization capability, but several recent retrospective studies have suggested that patients admitted to tertiary care hospitals capable of performing these procedures have better clinical outcomes (1–5). Similarly, small randomized trials of primary percutaneous transluminal coronary angioplasty (PTCA) versus fibrinolytic therapy have shown better outcomes with PTCA, a treatment available only at tertiary care hospitals (6). Other studies have shown improved quality of life, but no survival advantage, with a treatment strategy using more invasive procedures (7–9), although one study did relate higher procedure rates in the U.S. versus Canada to a trend of better survival (10). These reports raise the question of whether routine transfer of patients to hospitals with coronary revascularization capability would improve outcomes.

The Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO-I) trial prospectively enrolled 41,021 patients with MI treated with fibrinolytic therapy in 1,081 hospitals in 15 countries (11,12). To evaluate the concept of regional heart-care centers further, we limited our analysis in this study to the patients enrolled in U.S. hospitals. Our purpose was to examine clinical outcomes in patients treated at hospitals with and without coronary revascularization capability. Additionally, we evaluated outcomes in patients who remained in hospitals without coronary revascularization capability compared with those transferred to hospitals with revascularization capability.

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Abbreviations and Acronyms

ACE = angiotensin-converting enzyme
CABG = coronary artery bypass grafting
CI = confidence interval
GUSTO-I = Global Utilization of Streptokinase and TPA (alteplase) for Occluded coronary arteries
GUSTO-IIb = Global Use of Strategies To Open occluded arteries in acute coronary syndromes
MI = myocardial infarction
NRMI = National Registry of Myocardial Infarction
OR = odds ratio
PTCA = percutaneous transluminal coronary angioplasty

METHODS

Study population. There were 25,515 patients from 660 U.S. hospitals enrolled in GUSTO-I between December 27, 1990, and February 22, 1993, with site information available. The details and primary end points of GUSTO-I have previously been reported (11,12). Briefly, patients with chest pain lasting ≥20 min but <6 h with ST-segment elevation in two contiguous electrocardiographic leads, and no contraindications for fibrinolytic therapy, were randomized to one of four fibrinolytic regimens: streptokinase (1.5 million U over 1 h) with intravenous heparin, streptokinase with subcutaneous heparin, accelerated alteplase (15-mg bolus followed by infusion at 0.75 mg/kg [ ≤50 mg] over 30 min and 0.5 mg/kg [ ≤35 mg] over the next hour) with intravenous heparin, or alteplase (1 mg/kg over 1 h [ ≤90 mg]) plus streptokinase (1 million U over 1 h) with intravenous heparin. Adjunctive therapy included ≥160 mg chewable aspirin as soon as possible followed by 160 to 325 mg/day. Subcutaneous heparin (12,500 U twice daily) was continued for seven days or until discharge. Intravenous heparin (5,000 U bolus, then 1,000 U/h, adjusted to maintain an activated partial thromboplastin time of 60 s to 85 s) was given for ≥48 h. Unless contraindicated, 10 mg intravenous atenolol was given in two divided doses followed by 50 to 100 mg/day orally. All other medications and invasive procedures were left to the discretion of the attending physician. The primary end point of the trial was all-cause mortality at 30 days.

Definitions. Hospital types were divided into those that performed PTCA and coronary artery bypass graft surgery (CABG) (n = 286) and those without coronary revascularization programs (n = 374). Recurrent ischemia was defined as symptoms, electrocardiogram changes, and/or new hypertension, pulmonary edema, or murmurs thought by the physician to represent myocardial ischemia. Reinfarction was defined as the presence of ≥2 of the following: recurrent ischemia ≥15 min duration, new ST- or T-wave changes or new Q-waves, a second elevation in cardiac enzymes above the upper limit of normal or by another 20% if already elevated, or angiographic occlusion of a previously documented patent coronary artery. Cardiogenic shock was defined as systolic blood pressure (BP) <90 mm Hg for ≥1 h that was not responsive to fluid administration alone, thought to be secondary to cardiac dysfunction, and associated with signs of hypoperfusion or a cardiac index ≤2.2 l/min/m².

Patient transfers were listed on the case report form as elective, emergency, or required for participation in the angiographic substudy (12). Patients transferred to hospitals with coronary revascularization capability within 6 h were assumed to be transferred primarily for rescue PTCA. Patients transferred between 6 h and 48 h were assumed to be transferred generally for treatment of recurrent ischemia or infarction. Finally, patients transferred after 48 h of admission were assumed to be transferred generally for elective procedures.

Data collection. Baseline demographics, medical history, medications, procedures, complications, and clinical events were collected prospectively on the case report form. A blinded central clinical events committee adjudicated all suspected strokes using prospectively defined criteria.

Data analysis. All analyses were performed with SAS software (SAS, Cary, North Carolina). Prospectively defined baseline and end point variables were compared within the analysis groups using a Pearson chi-square test for categorical variables and a Wilcoxon rank-sum test for continuous variables. All categorical measures are reported as counts with percentages. All continuous measures are reported as medians for measures of centrality and 25th and 75th percentiles as measures of variation.

A previously validated and published model of 30-day death (13) found several factors statistically significant in a multivariable model. However, five of these factors (age, systolic BP, heart rate, Killip class, and MI location) jointly made up approximately 90% of the total chi-square (13); therefore, these five factors are used as the baseline factors for adjustment. We also tested all factors from the published model, and no differences in interpretations were found, so only models using the main five factors as confounders are reported.

Logistic regression modeling was used to assess the relationship between each of the groups (transfer status and revascularization capability) and death after adjusting for the five baseline factors. This process was used for both 30-day and one-year mortality. The interactions of each of the five factors with the groups were also tested to see if the association of transfer status (or revascularization capability) and mortality changed according to the levels of the baseline variables. Age, systolic BP, and heart rate were used as continuous measures in both the main effects and interaction terms. The continuous variables that were found to have statistically significant interactions were divided into two discrete groups for descriptive purposes only. The unadjusted rates of mortality within the baseline and analysis subgroups are generated to illustrate the differential...
Intravenous nitrates 10,803 (88.1%) 10,507 (79.6%) 0.001 4,578 (88.1%) 5,929 (74.0%) 0.001
Aspirin 11,399 (93.3%) 12,119 (92.3%) 0.002 4,881 (94.5%) 7,238 (90.9%) 0.001

between the two groups.

class or history of diabetes, smoking, MI, stroke, or CABG
transferred (Table 1). There were no differences in Killip
demia, prior angina, and prior PTCA than patients not
male, and had a higher incidence of hypertension, dyslipi-
disease, or prior stroke. Patients treated at hospitals with

insulin-converting enzyme.

angiotensin-converting enzyme (ACE) inhibitors. The use
oral or topical nitrates, intravenous beta-blockers, or
angiotensin-converting enzyme (ACE) inhibitors. The use

Medical treatment. The use of aspirin, intravenous ni-
trates, calcium-channel blockers, digitalis, and intravenous
inotropic agents was significantly greater in patients treated
at hospitals with revascularization capability, although the
absolute difference was only 1% for the use of aspirin (Table
2). Oral beta-adrenergic blocking agents were used slightly
more often in patients treated at hospitals without revascu-
larization capability. There were no differences in the use
of oral or topical nitrates, intravenous beta-blockers, or
angiotensin-converting enzyme (ACE) inhibitors. The use
of all medications was higher in patients transferred from
hospitals without coronary revascularization capability than
in patients not transferred.

Complications. The incidence of most complications after
MI was similar in the two types of hospitals (Table 3).
Second- or third-degree atrioventricular block occurred
more often, whereas acute mitral regurgitation occurred less
often, in patients treated at hospitals with revascularization
capability.

Patients transferred from hospitals without revasculariza-
tion capability had a higher incidence of atrial fibrillation or
flutter and acute mitral regurgitation, and a lower incidence
of asystole, than patients not transferred (Table 3). There

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Hospitals With Revascularization Capability (n = 12,279)</th>
<th>Hospitals Without Revascularization Capability (n = 13,236)</th>
<th>p Value</th>
<th>Transfer Patients (n = 5,218)</th>
<th>Non-Transfer Patients (n = 8,018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>60.7 (51.4, 69.5)</td>
<td>61.4 (51.8, 70)</td>
<td>0.002</td>
<td>60.4 (51.1, 68.7)</td>
<td>62.1 (52.3, 70.9)</td>
</tr>
<tr>
<td>Male</td>
<td>8,980 (73.2%)</td>
<td>9,682 (73.2%)</td>
<td>0.97</td>
<td>3,898 (74.8%)</td>
<td>5,784 (72.2%)</td>
</tr>
<tr>
<td>Killip class ≥ III</td>
<td>232 (1.9%)</td>
<td>251 (1.9%)</td>
<td>0.99</td>
<td>85 (1.6%)</td>
<td>166 (2.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5,172 (42.3%)</td>
<td>5,404 (41.0%)</td>
<td>0.04</td>
<td>2,204 (42.4%)</td>
<td>3,200 (40.1%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1,981 (16.2%)</td>
<td>2,172 (16.5%)</td>
<td>0.55</td>
<td>820 (15.7%)</td>
<td>1,352 (16.9%)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>5,315 (43.5%)</td>
<td>5,589 (42.5%)</td>
<td>0.08</td>
<td>2,165 (41.6%)</td>
<td>3,424 (43.0%)</td>
</tr>
<tr>
<td>Elevated cholesterol</td>
<td>4,511 (37.8%)</td>
<td>4,618 (36.4%)</td>
<td>0.02</td>
<td>2,021 (40.2%)</td>
<td>2,597 (33.9%)</td>
</tr>
<tr>
<td>Family history CAD</td>
<td>5,712 (48.7%)</td>
<td>5,987 (47.9%)</td>
<td>0.18</td>
<td>2,497 (50.4%)</td>
<td>3,490 (46.2%)</td>
</tr>
<tr>
<td>Prior angina</td>
<td>4,513 (37.0%)</td>
<td>4,482 (34.1%)</td>
<td>0.001</td>
<td>1,899 (36.6%)</td>
<td>2,583 (32.4%)</td>
</tr>
<tr>
<td>Prior infarction</td>
<td>2,181 (17.8%)</td>
<td>2,165 (16.4%)</td>
<td>0.003</td>
<td>864 (16.6%)</td>
<td>1,301 (16.3%)</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>281 (2.3%)</td>
<td>307 (2.3%)</td>
<td>0.88</td>
<td>113 (2.2%)</td>
<td>194 (2.4%)</td>
</tr>
<tr>
<td>Prior angioplasty</td>
<td>752 (6.1%)</td>
<td>589 (4.5%)</td>
<td>0.001</td>
<td>282 (5.4%)</td>
<td>307 (3.8%)</td>
</tr>
<tr>
<td>Prior bypass surgery</td>
<td>783 (6.4%)</td>
<td>601 (4.6%)</td>
<td>0.001</td>
<td>251 (4.8%)</td>
<td>350 (4.4%)</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme.

Association. The odds ratios (OR) with 95% confidence
intervals (CI) illustrate the adjusted interactions.

A p value < 0.01 instead of < 0.05 was considered
statistically significant because of the large numbers
of patients and the multiple comparisons.

RESULTS

Baseline characteristics. Patients treated at hospitals with
coronary revascularization capability were significantly
younger than those treated at hospitals without revascular-
zation capability (Table 1). There were no significant
differences in gender, Killip class, hypertension, diabetes
mellitus, smoking, dyslipidemia, family history of coronary
disease, or prior stroke. Patients treated at hospitals with
coronary revascularization capability had a higher incidence
of prior angina, MI, PTCA, and CABG.

Patients transferred from hospitals without coronary revas-
cularization capability were younger, were more often
male, and had a higher incidence of hypertension, dysli-
pidemia, prior angina, and prior PTCA than patients not
transferred (Table 1). There were no differences in Killip
class or history of diabetes, smoking, MI, stroke, or CABG
between the two groups.

Table 2. Treatments Received

<table>
<thead>
<tr>
<th>Drug Therapies</th>
<th>Hospitals With Revascularization Capability</th>
<th>Hospitals Without Revascularization Capability</th>
<th>p Value</th>
<th>Transfer Patients</th>
<th>Non-Transfer Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>11,399 (93.3%)</td>
<td>12,119 (92.3%)</td>
<td>0.002</td>
<td>4,881 (94.5%)</td>
<td>7,238 (90.9%)</td>
</tr>
<tr>
<td>Intravenous nitrates</td>
<td>10,803 (88.1%)</td>
<td>12,119 (92.3%)</td>
<td>0.001</td>
<td>4,578 (88.1%)</td>
<td>4,728 (90.9%)</td>
</tr>
<tr>
<td>Oral or topical nitrates</td>
<td>8,715 (71.1%)</td>
<td>9,531 (71.1%)</td>
<td>0.94</td>
<td>3,921 (76.1%)</td>
<td>5,430 (67.9%)</td>
</tr>
<tr>
<td>Intravenous beta-blockers</td>
<td>6,560 (53.5%)</td>
<td>6,913 (52.3%)</td>
<td>0.06</td>
<td>2,852 (54.9%)</td>
<td>4,061 (50.7%)</td>
</tr>
<tr>
<td>Oral beta-blockers</td>
<td>8,980 (73.2%)</td>
<td>9,894 (75.0%)</td>
<td>0.002</td>
<td>3,945 (76.0%)</td>
<td>5,949 (74.3%)</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>4,735 (38.6%)</td>
<td>4,409 (33.5%)</td>
<td>0.001</td>
<td>2,244 (43.5%)</td>
<td>2,165 (27.1%)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>2,559 (20.9%)</td>
<td>2,647 (20.2%)</td>
<td>0.15</td>
<td>1,086 (21.2%)</td>
<td>1,559 (19.5%)</td>
</tr>
<tr>
<td>Digitalis</td>
<td>2,189 (17.9%)</td>
<td>1,947 (14.8%)</td>
<td>0.001</td>
<td>949 (18.4%)</td>
<td>998 (12.5%)</td>
</tr>
<tr>
<td>Other inotropic agents</td>
<td>3,027 (24.7%)</td>
<td>2,669 (20.3%)</td>
<td>0.001</td>
<td>1,241 (24.1%)</td>
<td>1,428 (17.9%)</td>
</tr>
</tbody>
</table>
were no differences in atrioventricular block, ventricular arrhythmias, acute ventricular septal rupture, cardiac tamponade, or Killip class.

**Procedures.** Patients at hospitals with coronary revascularization capability were more likely to undergo mechanical ventilation, pulmonary artery catheterization, temporary pacemaker placement, intra-aortic balloon counterpulsation, angiography, PTCA, and CABG (Table 4).

Patients transferred from hospitals without coronary revascularization capability almost always had angiography and more often underwent other invasive procedures (Table 4). Patients remaining in such hospitals were less likely to undergo an invasive procedure. The indication for angiography was available in 4,847 of 5,218 patients; it was performed emergently in 1,006 patients (20.8%), electively in 3,681 (75.9%), and as required by the angiographic substudy protocol in 160 patients (3.3%). Similarly, data were available for 3,325 of 5,218 patients regarding time to transfer: 206 patients (6.2%) were transferred within 6 h, 496 (14.9%) between 6 h and 48 h, and the remaining 2,623 (78.9%) after 48 h.

**Clinical events.** The rates of recurrent ischemia, reinfarction, congestive heart failure, shock, and stroke did not differ between the two hospital types (Table 5). Patients in hospitals with revascularization capability had 30-day mortality risk similar to that of patients in hospitals without revascularization capability (OR 0.91, 95% CI 0.82 to 1.0). After adjustment for age, systolic BP, heart rate, baseline Killip class, and MI location, 30-day mortality remained similar for patients treated at hospitals with revascularization capability compared with those treated at hospitals without revascularization capability (OR 0.91, 95% CI 0.82 to 1.02). The unadjusted (OR 0.96, 95% CI 0.89 to 1.05) and adjusted (OR 0.98, 95% CI 0.90 to 1.07) one-year mortality rates were also similar between the two hospital types. The 30-day (adjusted OR 0.95, 95% CI 0.79 to 1.14) and one-year (adjusted OR 1.06, 95% CI 0.91 to 1.23) mortality rates were similar among patients <65 years of age treated at hospitals with revascularization capability compared with those treated at hospitals without revascularization capability. Likewise, the 30-day (adjusted OR 0.90, 95% CI 0.79 to 1.02) and one-year (adjusted OR 0.94, 95% CI 0.85 to 1.05) mortality rates were similar among patients ≥65 years of age treated at hospitals with revascularization capability compared with those treated at hospitals without revascularization capability.

Patients transferred from hospitals without revascularization capability had a higher incidence of recurrent ischemia, recurrent infarction, and congestive heart failure than non-transfer patients but equivalent rates of shock and stroke (Table 5). Unadjusted 30-day (OR 0.38, 95% CI 0.32 to 0.44) and one-year (OR 0.46, 95% CI 0.40 to 0.52) mortality rates were significantly lower for transfer patients. After adjustment for differences in baseline predictors of 30-day and one-year mortality, these still remained significantly lower for transfer versus non-transfer patients (Table 5).
Table 5. Clinical Events

<table>
<thead>
<tr>
<th>Events</th>
<th>Hospitals With Revascularization Capability</th>
<th>Hospitals Without Revascularization Capability</th>
<th>p Value</th>
<th>Transfer Patients</th>
<th>Non-Transfer Patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent ischemia</td>
<td>2,728 (22.3%)</td>
<td>3,034 (23.0%)</td>
<td>0.14</td>
<td>1,783 (34.4%)</td>
<td>1,251 (15.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>457 (3.7%)</td>
<td>517 (3.9%)</td>
<td>0.42</td>
<td>338 (6.5%)</td>
<td>179 (2.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2,176 (17.8%)</td>
<td>2,387 (18.1%)</td>
<td>0.46</td>
<td>997 (19.3%)</td>
<td>1,390 (17.4%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Shock</td>
<td>833 (6.8%)</td>
<td>881 (6.7%)</td>
<td>0.71</td>
<td>354 (6.8%)</td>
<td>527 (6.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>187 (1.5%)</td>
<td>199 (1.5%)</td>
<td>0.91</td>
<td>72 (1.4%)</td>
<td>127 (1.6%)</td>
<td>0.36</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>766 (6.2%)</td>
<td>903 (6.8%)</td>
<td>0.06</td>
<td>184 (3.5%)</td>
<td>719 (9.0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>802 (6.6%)</td>
<td>949 (7.2%)</td>
<td>0.04</td>
<td>196 (3.8%)</td>
<td>753 (9.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>One-year mortality</td>
<td>1,177 (9.6%)</td>
<td>1,313 (9.9%)</td>
<td>0.37</td>
<td>318 (6.1%)</td>
<td>995 (12.4%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

0.45, 95% CI 0.38 to 0.54] and [OR 0.54, 95% CI 0.47 to 0.63], respectively). These results are probably biased by the fact that patients who died early were obviously not candidates for transfer. The excess of asystolic events (679 vs. 204, p < 0.001) in the non-transfer group supports this hypothesis. Similarly, mortality at 30-days and one-year was significantly lower in both transfer patients age <65 and ≥65 years.

**DISCUSSION**

In this large study, patients with acute MI treated with fibrinolytic therapy and admitted to hospitals with and without coronary revascularization capability had similar outcomes when appropriate candidates received aspirin and beta-blockers, and immediate transfer was available for angiography and angioplasty as needed. Although the non-significant lower 30-day adjusted mortality in hospitals with coronary revascularization capability does not exclude a modestly better outcome in these hospitals, lack of substantial advantage is more likely, given the one-year results. Further, there was no difference in 30-day and one-year mortality between the two hospital types in patients age <65 or ≥65 years. These results are consistent with prior observations that immediate availability of invasive procedures is not associated with a survival advantage (4,14–19).

**Hospitals with and without coronary revascularization capability.** Although there were a few statistically significant differences in baseline characteristics and complications due to the large sample size, there were no major clinical differences in patients admitted to hospitals with and without coronary revascularization capability. This would be expected given the current practice of transporting patients to the nearest hospital for chest pain evaluation. There was a statistically and clinically significant increase in number of procedures performed at hospitals with revascularization capability, however, as has been documented previously (14,15,20,21).

Better outcomes have been shown for patients with MI treated at teaching hospitals (1,3,5), at top-ranked hospitals (2), and by cardiologists (22–24). Additionally, higher physician volume (24), primary PTCA volume (25), and hospital volume (4) predict better outcomes for patients with MI. Patients in these situations are more likely to be treated with medications associated with improved survival (aspirin, beta-blockers, and ACE inhibitors) (2,5) and with interventional procedures performed by highly skilled teams. These different descriptors most likely represent important measures of quality of care.

Kizer et al. (26) found that physicians who design or implement randomized clinical trials are more likely to use aspirin, beta-blockers, and ACE inhibitors than physicians in routine clinical practice. Patients in this study enrolled in hospitals without revascularization capability were treated with the same protocol as were patients enrolled in hospitals with revascularization capability, and they had similar clinical outcomes, including 30-day and one-year mortality, despite undergoing fewer procedures. These results suggest that the ability to successfully implement a randomized clinical trial protocol or to follow an evidence-based MI treatment protocol should represent another measure of quality of care.

**Interhospital transfer.** Most previous observational database studies analyzing discharge diagnoses have excluded transfer patients (4,5,24). Likewise, patients admitted as transfers from other hospitals were omitted from the second National Registry of Myocardial Infarction (NRMI-2) analyses (15,25). In this study, 40% of patients treated with fibrinolytic therapy in hospitals without revascularization capability were transferred to hospitals with this capability. Eighty percent of the transfers occurred ≥48 h after hospital admission; fewer than 10% of transfers occurred within a time window where rescue PTCA might be performed. The overwhelming indication for transfer appeared to be referral for angiography, which was performed in 94% of patients. Ischemic complications, not cardiogenic shock or ventricular arrhythmias, were more common in these patients.

Transfer patients received more pharmacologic therapy, underwent more procedures, and had lower unadjusted and adjusted mortality rates than patients who were not transferred. They were a selected group of patients, however. Most had survived the initial 24 h of hospitalization, within which 40% of the deaths occurred in this study (27). Thus, immediate treatment with fibrinolytic therapy along with other appropriate medical regimens, initial stabilization, early risk stratification, and selective referral by physicians at...
hospitals without coronary revascularization capability appeared to produce outcomes similar to those achieved in hospitals where revascularization was available, with fewer procedures performed.

On-site cardiac catheterization facility. No difference in mortality has been reported for patients treated at hospitals with on-site cardiac catheterization facilities (4,14–19) or in geographic regions with higher rates of intervention (7,10,28,29). Moreover, Canto et al. (25) found 28% lower mortality among patients who underwent primary PTCA at hospitals with high volumes versus hospitals with low volumes, but no relationship between volume of fibrinolytic interventions and hospital mortality. Our results are similar to these findings and support the concept that as long as access to PTCA or CABG is available, it need not be immediately available to maintain the initial benefits of fibrinolysis.

Although older randomized trials found superiority for PTCA over streptokinase (30) and over 3-h alteplase infusions (31), when time to treatment was <1 h, no mortality benefit was seen in the NRMI-2 registry reports, where door-to-balloon time was 2 h (32,33). Only 8% of patients in the NRMI-2 registry (33) were treated with PTCA within 1 h, and accelerated alteplase was the predominant fibrinolytic agent.

The GUSTO-IIIb PTCA substudy (34) is the only prospective randomized comparison of accelerated alteplase dosing versus PTCA. No difference in outcome was seen for six days, suggesting that the small treatment benefit with PTCA at 30 days was due to reduced reocclusion rates rather than to better reperfusion rates.

Despite claims by some that higher patency rates achieved with PTCA will result in better outcomes and thus justify delaying treatment until it can be performed, several recent reports have clearly shown that delayed PTCA is associated with decreased myocardial salvage and increased mortality rates (33,35,36), just as with fibrinolytic therapy. Nevertheless, studies in the Netherlands, Denmark, France, and the Czech Republic are testing the strategies of delayed reperfusion with transfer to a tertiary-care hospital for PTCA versus immediate fibrinolysis in community hospitals. An attempt to test this hypothesis in the U.S. was aborted after three years because of poor patient recruitment (37). There was a 100-min delay in time to treatment with PTCA and no difference in outcome.

Study limitations. First, this study included only patients with ST-segment elevation who were treated with fibrinolytic therapy. These results may not apply to patients not receiving fibrinolytic therapy, where the immediate availability of reperfusion therapy with PTCA could offer an advantage. However, previous studies including patients with ST-segment depression or PTCA treatment availability found no survival advantage at hospitals with coronary revascularization capability (4,14–19). Neither does our study evaluate whether immediate referral for primary or facilitated PTCA is a better reperfusion strategy. Second, this analysis is based on a post-hoc review of a study enrolling patients from 1990 to 1992. However, recent innovations including newer fibrinolytic agents (38,39), newer antithrombotic agents in combination with fibrinolytic agents (40,41), and coronary stents (42,43) have not been shown to further reduce mortality from MI. Third, even with over 25,000 patients, the power to detect a significant difference in outcome is low, especially in light of potential unmeasured confounding factors. The 0.6% higher mortality rate at 30 days in hospitals without revascularization facilities, while not statistically significant at a p <0.01 level after adjustment for baseline differences, includes the possibility of as much as an 18% relative reduction in mortality within the 95% confidence interval. Fourth, although we have used multivariable modeling to adjust for baseline risk, the results of this type of observational study may be confounded by unmeasured variables. With this limitation and the retrospective observational nature of this analysis, our results should be considered hypothesis generating rather than conclusive. Finally, these results do not apply to patients in cardiogenic shock, where emergency PTCA has been shown to reduce mortality (44). Appropriate patients in cardiogenic shock should be transferred immediately to hospitals capable of performing PTCA and CABG.

Conclusions. This study suggests similar outcomes for patients treated with fibrinolytic therapy at hospitals with and without coronary revascularization capability, provided that appropriate candidates receive aspirin and beta-blockers, and that transfer is available for angiography and coronary revascularization as needed.

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