

# Use of the Electrocardiograph-Based Thrombolytic Predictive Instrument To Assist Thrombolytic and Reperfusion Therapy for Acute Myocardial Infarction

## A Multicenter, Randomized, Controlled, Clinical Effectiveness Trial

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**Background:** Deciding which patients should receive thrombolytic therapy or percutaneous transluminal coronary angioplasty (PTCA) for acute myocardial infarction (AMI) can be difficult, especially for less-obvious candidates and when consulting physicians are off site.

**Objective:** To test whether the electrocardiograph-based Thrombolytic Predictive Instrument (TPI) improves use of thrombolytic and overall reperfusion therapy.

**Design:** 22-month randomized, controlled, clinical effectiveness trial.

**Setting:** Emergency departments at 28 urban, suburban, and rural hospitals in the United States.

**Patients:** Persons presenting to the emergency department with AMI and ST-segment elevation on an electrocardiogram (ECG).

**Intervention:** TPI predictions automatically printed on ECG text headers.

**Measurements:** Percentages of patients receiving thrombolytic therapy, thrombolytic therapy within 1 hour of initial ECG, and overall reperfusion (thrombolytic therapy or PTCA).

**Results:** Of 2875 patients with AMI, 1243 (43.2%) had ST-segment elevation. Of these, 1197 were randomly assigned to study groups; 732 (61.2%) had inferior AMI, and 465 (38.8%) had anterior AMI. A total of 60.5% of controls and 62.1% of TPI patients ( $P = 0.2$ ) received thrombolytic therapy, 52.5% of controls and 53.3% of TPI patients received thrombolytic therapy within 1 hour ( $P > 0.2$ ), and 67.6% of controls and 70.3% of TPI patients received overall reperfusion ( $P = 0.2$ ). Of patients with

inferior AMI in the control group versus the TPI group, 61.1% versus 67.6% ( $P = 0.03$ ) received thrombolytic therapy, 53.2% versus 58.6% ( $P = 0.08$ ) received thrombolytic therapy within 1 hour, and 67.7% versus 74.7% ( $P = 0.03$ ) received overall reperfusion. Of patients with anterior AMI in the control group versus the TPI group, 59.5% versus 53.9% ( $P > 0.2$ ) received thrombolytic therapy, 51.4% versus 45.3% ( $P > 0.2$ ) received thrombolytic therapy within 1 hour, and 67.6% versus 63.8% ( $P > 0.2$ ) received overall reperfusion. Among women ( $n = 398$ ) in the control group versus the TPI group, 48.1% versus 58.2% ( $P = 0.03$ ) received thrombolytic therapy, 40.5% versus 48.4% ( $P = 0.10$ ) received thrombolytic therapy within 1 hour, and 55.7% versus 65.7% ( $P = 0.04$ ) received overall reperfusion. Of patients who required physician consultation by telephone ( $n = 271$ ) in the control group versus the TPI group, 47.3% versus 63.2% ( $P = 0.01$ ) received thrombolytic therapy, 41.1% versus 53.6% ( $P = 0.04$ ) received thrombolytic therapy within 1 hour, and 50.7% versus 66.4% ( $P = 0.01$ ) received overall reperfusion.

**Conclusions:** The TPI increased use of thrombolytic therapy, use of thrombolytic therapy within 1 hour, and use of overall coronary reperfusion by 11% to 12% for patients with inferior AMI, 18% to 22% for women, and 30% to 34% for patients with an off-site physician. Although its effect was minimal on patients with high baseline reperfusion rates, the TPI increased use and timeliness of reperfusion in often-missed groups and when involved physicians were off site.

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**E**mergent coronary reperfusion for acute myocardial infarction (AMI) can be lifesaving for appropriate patients who are promptly recognized and treated (1–4). However, in the emergency department setting, this prompt recognition can be difficult, especially for less-obvious candidates and when physician decision makers are not all on site. To assist in treatment decisions, the Thrombolytic Predictive Instrument (TPI), incorporated into conventional computerized electrocardiography, prints on the electrocardiogram (ECG) text header its predictions of key outcomes of thrombolytic therapy: 30-day mortality, 1-year mortality, cardiac arrest, hemorrhagic stroke, and bleeding requiring transfusion (5, 6).

Over the past decade, as a result of intensive efforts by physician leaders, the U.S. National Institutes of Health National Heart Attack Alert Program, organizations inter-

ested in quality of medical care, the pharmaceutical industry, and others (3, 7–16), more patients with AMI have received thrombolytic therapy and have received it sooner (17). However, further improvement is needed (17–20), especially for patients with AMI other than anterior AMI (the category of AMI for which thrombolytic therapy was first recognized as effective [1, 2]) and for women (who have received reperfusion therapy at lower rates than men [18, 20]). Also needed are ways to support prompt, accurate decisions about reperfusion therapy in hospitals and in prehospital emergency medical service (EMS) settings where consultation with off-site physicians may be required. The need for prompt recognition of potential benefit also applies to acute reperfusion by primary percutaneous transluminal coronary angioplasty (PTCA), which may be equivalent to thrombolytic therapy or even preferable

**Context**

Decision making about thrombolysis in acute myocardial infarction (AMI) can be difficult. The Thrombolytic Predictive Instrument (TPI) estimates the risk for death and hemorrhage with and without thrombolysis. Its effect on patient care is unknown.

**Contribution**

This randomized trial of the TPI in emergency departments showed that printing TPI predictions on the admission electrocardiogram increased the frequency of reperfusion for inferior AMI but not anterior AMI. The effect of the TPI was greatest for women and for patients who required off-site consultation.

**Implications**

The TPI is a tool to assure all patients the same standard of care.

—The Editors

for some patients with AMI (21–25). Thus, any method of increasing use of thrombolytic therapy should not interfere with the alternative use of PTCA, when indicated.

To test whether the TPI addresses these needs, we did a randomized, controlled, clinical effectiveness trial in the emergency departments of 28 diverse hospitals. We sought to determine whether the TPI would help physicians 1) identify patients needing thrombolytic therapy who would not otherwise have been identified; 2) use thrombolytic therapy sooner; 3) identify more candidates for overall coronary reperfusion, including medical thrombolysis or primary PTCA; and 4) expedite decisions about reperfusion when physician decision makers are not all on site.

**METHODS****Study Sites**

Our study was done in 28 U.S. hospitals, including public, private, community, and tertiary care hospitals in urban, suburban, and rural areas: Bess Kaiser Medical Center (Portland, Oregon), Boston City Hospital (Boston, Massachusetts), Box Butte General Hospital (Alliance, Nebraska), Carney Hospital (Dorchester, Massachusetts), Cedars-Sinai Medical Center (Los Angeles, California), Chadron Community Hospital (Chadron, Nebraska), Cooley Dickinson Hospital (Northampton, Massachusetts), Decatur County Hospital (Oberlin, Kansas), Franklin Medical Center (Greenfield, Massachusetts), Huntington Hospital (Huntington, New York), Lincoln Community Hospital (Hugo, Colorado), Mary Lane Hospital (Ware, Massachusetts), Memorial Health Center (Sidney, Nebraska), Memorial Hospital (Craig, Colorado), New England Medical Center (Boston, Massachusetts), Noble Hospital (Westfield, Massachusetts), North Shore University Hospital—Glen Cove (Glen Cove, New York), Plains Medical Center

(Limon, Colorado), Presbyterian/St. Luke's Medical Center (Denver, Colorado), Regional West Medical Center (Scottsbluff, Nebraska), Rhode Island Hospital (Providence, Rhode Island), Silverheels Health Center (Fairplay, Colorado), Southeast Colorado Hospital (Springfield, Colorado), Sunnyside Medical Center (Clackamas, Oregon), Swedish Hospital (Engelwood, Colorado), Timberline Medical Center (Granby, Colorado), University Hospital (Boston, Massachusetts), and University Hospital—Stony Brook (Stony Brook, New York).

**Patients and Intervention**

We included all consenting patients 35 years of age and older who 1) presented with AMI to any study hospital during the 22-month period beginning 24 April 1995 and 2) had, on presentation to the emergency department, detection of ST-segment elevation characteristic of AMI on an ECG.

At study hospitals, software that generated the TPI predictions was installed on conventional computerized electrocardiographs (Hewlett-Packard, Palo Alto, California) so that ST-segment elevation characteristic of AMI was automatically detected. When this elevation was detected, the patient was automatically randomly assigned to the control or the TPI group. Randomization did not delay obtaining an ECG or treatment. (In accordance with Institutional Review Board approval [given that usual ECGs and ECGs with TPI predictions both represent standard care and that it is necessary not to disrupt initial emergency care], we obtained written informed consent as soon as was practical after the initial ECG.) For patients in the TPI group, the electrocardiograph automatically prompted the user to enter patient information needed to make the TPI predictions: age, sex, history of hypertension, history of diabetes, blood pressure, and time since onset of ischemic symptoms. The remaining variables, based on measurement of ECG waveforms, were automatically acquired by the electrocardiograph. Then the ECG was printed with the TPI predictions on its header. If any variables for the calculations were missing, predictions were not calculated and an alert listing the missing variables was printed. Entry of missing data, if available, was allowed. Predictions were not generated for patients older than 75 years of age (5, 26, 27). For controls, the ECG was automatically printed with the header text customarily used in that emergency department.

**Data Collection and Analysis**

At presentation and during hospitalization, we collected sociodemographic information; data on clinical features, ECGs, and all cardiac biomarker test results (at minimum, serial creatine kinase MB tests) at presentation and follow-up; the triaging physician's training level and specialty and whether he or she was emergency department-based; whether on- or off-site (telephone) consultations were used in making the reperfusion treatment decision; whether the patient received thrombolytic therapy and, if

so, the time from onset of chest pain to receipt of therapy; and whether the patient received primary PTCA. The TPI software allowed real-time acquisition of the clinical variables required for the TPI calculations and automatic acquisition of Q-wave, ST-segment, and T-wave measurements. Follow-up data needed to assign confirmed “true” diagnoses were collected from arrival at the emergency department through the 30-day follow-up visit. The overall 30-day follow-up rate was 100%.

Site physicians, blinded to study group assignments, used World Health Organization criteria (28) to assign confirmed diagnoses on the basis of presentation, clinical course, initial and follow-up ECGs, and biomarker tests. An AMI was classified as anterior if the patient had at least two contiguous ECG anterior leads with ST-segment elevation, regardless of whether this was accompanied by elevation elsewhere. Any AMI with no significant anterior ST-segment elevation was classified as inferior. Emergency department care was classified by whether consultation with an off-site physician was used in making the treatment decision. Hospital size, hospital type, presence of on-site emergency department staff, and physician type were used as potentially explanatory variables.

### Statistical Analysis

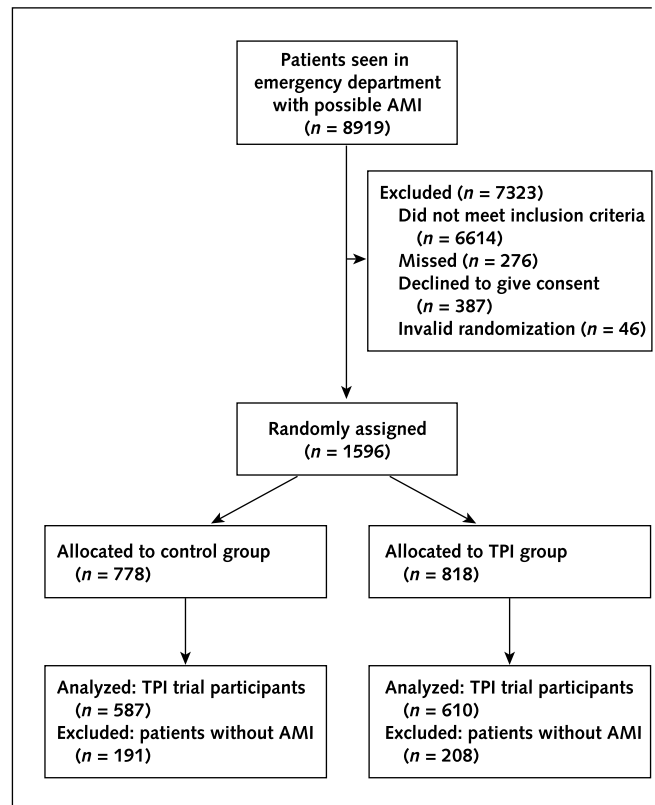
Baseline comparisons of patient characteristics between the control and TPI groups were done by using *t*-tests for continuous variables and chi-square tests for categorical variables. Because of skewed distributions of times from symptom onset, median times from symptom onset to initial ECG were compared between groups by using the Wilcoxon rank-sum test. Chi-square tests for  $2 \times 2$  tables were used to compare crude differences between groups in rates of use of thrombolytic therapy; use of thrombolytic therapy within 1 hour of randomization; and overall use of reperfusion, including PTCA. The predictive discrimination of the TPI’s mortality predictions was measured by using the area under the receiver-operating characteristic (ROC) curve, estimated by the *c* statistic from the logistic regression model predicting the outcome with the predicted values as the sole independent variable.

Relative risks and *P* values were derived from the  $2 \times 2$  tables and chi-square tests. Analyses by AMI location and patient sex were also adjusted for hospital type (urban teaching hospital, teaching-affiliated hospital, or community or rural hospital) by using the Cochran–Mantel–Haenszel test. Hospital groupings were made before analyses were done and reflect similar characteristics and expected reperfusion rates. Commonality of the relative risk across hospital type was tested by using the Breslow–Day chi-square statistic. We used SAS, version 8 (SAS, Inc., Cary, North Carolina) for all analyses.

### Role of the Funding Source

Neither the funding source nor the manufacturers of equipment or software had any role in the collection, analysis, or interpretation of data or in the writing or submission

Figure. Patient inclusion.



AMI = acute myocardial infarction; TPI = Thrombolytic Predictive Instrument.

of this paper for publication. Primary data analyses, including breaking of the randomization code, were done first by an outside independent statistician on the Data Monitoring and Safety Committee.

### RESULTS

As shown in the Figure, a total of 8919 patients with possible AMI were screened for study eligibility. Of 3266 eligible patients with AMI, 2879 (88%) consented to participate; 1237 (43%) had AMI with ST-segment elevation detected and were randomly assigned to study groups by the electrocardiograph. Of these 1237 patients, 40 (3.2%) had two different randomization assignments and thus were excluded from the trial. Of the 1197 patients included in the trial, those assigned to the control group ( $n = 587$ ) and those assigned to the TPI group ( $n = 610$ ) were similar, except for trends toward more previous coronary artery disease in the control group and more diabetes in the TPI group (Table 1). The 1642 consenting patients with AMI without ST-segment elevation were included in a “non-trial” registry.

For safety, we monitored patients who had ST-segment elevation detected but did not have AMI. The control group had 191 such patients, of whom 1 (0.5%) received thrombolytic therapy; the TPI group had 208 such

**Table 1. Presenting Characteristics of Patients with Acute Myocardial Infarction Who Were Randomly Assigned to Study Groups\***

Characteristic	Control Group (n = 587)	TPI Group (n = 610)	P Value
Mean age, y	63.8	63.6	>0.2
Male sex, %	68.5	65.1	0.2
Ethnicity, %			
White	91.7	91.6	
Black	4.1	4.8	>0.2
Hispanic	2.7	2.0	
Other	1.5	1.6	
Mean systolic blood pressure	142.9	142.4	>0.2
Median time from onset of symptoms to arrival at the emergency department (25th, 75th percentile), min	142 (81, 279)	131 (79, 265)	>0.2
Clinical features, %			
History of hypertension	50.9	51.0	>0.2
History of coronary artery disease	37.8	34.1	0.18
History of diabetes	18.2	22.5	0.07
Previous MI	27.8	24.1	0.15
Anterior acute MI	37.8	39.8	>0.2
Previous thrombolytic therapy	5.7	6.8	>0.2
Previous stroke	5.6	4.1	>0.2

\* MI = myocardial infarction; TPI = Thrombolytic Predictive Instrument.

patients, of whom 3 (1.4%) received thrombolytic therapy ( $P > 0.2$ ). We also monitored use of thrombolytic therapy in patients with contraindications; the control group had two such patients (0.6%), and the TPI group had one (0.3%) ( $P > 0.2$ ). The rate of use of thrombolytic therapy for study patients was 69.0%. Use varied by type of hospital, with observed rates of 46.3%, 73.5%, and 70.5% in urban teaching, teaching-affiliated, and rural or community hospitals, respectively. Across all hospitals, 52.9% of patients received thrombolytic therapy within 1 hour (39.8% at urban teaching hospitals, 65.0% at teaching-affiliated hospitals, and 59.0% at rural or community hospitals). The rate of overall reperfusion, including thrombolytic therapy or primary PTCA, was 62.8% at urban teaching hospitals, 74.3% at teaching-affiliated hospitals,

and 72.5% at rural or community hospitals. Neither patient sex nor AMI location differed significantly by hospital type.

Table 2 shows that printing TPI predictions on the ECG significantly improved reperfusion rates for inferior, but not anterior, AMIs. Among the 732 patients (61.2%) with inferior AMI, 61.1% of those in the control group and 67.6% of those in the TPI group received thrombolytic therapy ( $P = 0.03$ ); 53.2% of those in the control group and 58.6% of those in the TPI group received this therapy within 1 hour ( $P = 0.08$ ). Rates of overall reperfusion (thrombolytic therapy or primary PTCA) were 67.7% in the control group and 74.7% in the TPI group ( $P = 0.03$ ). These absolute changes of 5 to 7 percentage points represent relative changes of 11% to 12%. Among the 465 trial patients (38.8%) with anterior AMI, no significant differences were seen between the control and TPI groups, as shown by relative risks of 0.9 to 1.0 ( $P > 0.2$ ) for each reperfusion treatment measure.

Table 3, in which patients with inferior and anterior AMIs are combined, shows the effect of the TPI in women and men. In women, TPI increased the rate of use of thrombolytic therapy from 48.1% to 58.2% ( $P = 0.03$ ), increased the rate of use of thrombolytic therapy within 1 hour from 40.5% to 48.4% ( $P = 0.10$ ), and increased the rate of use of overall reperfusion from 55.7% to 65.7% ( $P = 0.04$ ). These absolute increases of 8 to 10 percentage points represent relative increases of 18% to 22%. In men, when those with inferior and those with anterior AMIs were combined, the effect of TPI was not significant.

Table 4 shows the effect of the TPI when telephone consultation with an off-site primary care physician or cardiologist was required. When consultation was done entirely by telephone ( $n = 271$ ), 47.3% of the control group and 63.2% of the TPI group received thrombolytic therapy ( $P = 0.01$ ), 41.1% of the control group and 53.6% of the TPI group received thrombolytic therapy within 1 hour ( $P = 0.04$ ), and 50.7% of the control group and 66.4% of the TPI group received overall reperfusion ( $P = 0.01$ ). These absolute changes of 13 to 16 percentage points represent relative changes of 30% to 34%. Consistent effects

**Table 2. Effect of the Thrombolytic Predictive Instrument on Treatment of Patients with Acute Myocardial Infarction by Location of Infarction\***

Patients	Treatment Received	Control Group (n = 587), %	TPI Group (n = 610), %	Relative Risk with TPI (95% CI)†	P Value†
All patients (n = 1197)	Thrombolytic therapy within 1 hour	52.5	53.3	1.0 (0.9–1.2)	>0.2
	Thrombolytic therapy	60.5	62.1	1.1 (0.96–1.1)	0.2
	Thrombolytic therapy or PTCA	67.6	70.3	1.0 (0.97–1.1)	0.2
Patients with inferior AMI (n = 732)	Thrombolytic therapy within 1 hour	53.2	58.6	1.1 (0.9–1.3)	0.08
	Thrombolytic therapy	61.1	67.6	1.1 (1.01–1.2)	0.03
	Thrombolytic therapy or PTCA	67.7	74.7	1.1 (1.01–1.2)	0.03
Patients with anterior AMI (n = 465)	Thrombolytic therapy within 1 hour	51.4	45.3	0.9 (0.8–1.1)	>0.2
	Thrombolytic therapy	59.5	53.9	0.9 (0.8–1.1)	>0.2
	Thrombolytic therapy or PTCA	67.6	63.8	1.0 (0.8–1.1)	>0.2

\* AMI = acute myocardial infarction; PTCA = primary percutaneous transluminal coronary angioplasty; TPI = Thrombolytic Predictive Instrument.

† Adjusted for type of hospital.

**Table 3. Effect of the Thrombolytic Predictive Instrument on Treatment of Patients with Acute Myocardial Infarction by Patient Sex\***

Patients	Treatment Received	Control Group (n = 587), %	TPI Group (n = 610), %	Relative Risk with TPI (95% CI)†	P Value‡
Women (n = 398)	Thrombolytic therapy within 1 hour	40.5	48.4	1.2 (0.96–1.5)	0.10
	Thrombolytic therapy	48.1	58.2	1.2 (1.01–1.5)	0.03
	Thrombolytic therapy or PTCA	55.7	65.7	1.2 (1.0–1.4)	0.04
Men (n = 799)	Thrombolytic therapy within 1 hour	58.0	55.9	1.0 (0.9–1.1)	>0.2
	Thrombolytic therapy	66.2	64.2	1.0 (0.9–1.1)	>0.2
	Thrombolytic therapy or PTCA	73.1	72.8	1.0 (0.9–1.1)	>0.2

\* PTCA = primary percutaneous transluminal coronary angioplasty; TPI = Thrombolytic Predictive Instrument.

† Adjusted for type of hospital.

were seen in separate subgroup analyses for telephone consultations with primary care physicians and cardiologists.

Table 5 shows the effect of TPI among the 56 patients seen at hospitals without on-site emergency department physicians. The small size of this group limits our ability to detect statistical significance, but the results show absolute increases of 18 to 26 percentage points in use of thrombolytic therapy, use of thrombolytic therapy within 1 hour, and overall reperfusion, representing relative increases of 44% to 53%. The TPI predictions of 30-day mortality were very good, as shown by the area under the ROC curve of 0.82 for all patients, 0.85 for recipients of thrombolytic therapy, and 0.84 for PTCA recipients. These models were also well calibrated, with similar agreement between observed and predicted mortality rates across the entire risk range.

Although this trial was not powered to detect significant differences in mortality and stroke rates, we monitored these outcomes for safety reasons. Overall mortality rates were 3.4% in the control group and 5.0% in the TPI group ( $P = 0.15$ ). When these rates were corrected for the higher rate of diabetes in the TPI group, again, they did not differ significantly ( $P > 0.2$ ). Three strokes each (0.5%) occurred in the control and TPI groups ( $P > 0.2$ ). Thrombolysis-related bleeding requiring transfusion occurred in 16 controls (4.5%) and 22 patients in the TPI group (5.8%) ( $P > 0.2$ ).

## DISCUSSION

This multicenter, controlled, clinical effectiveness trial tested the effect of having an electrocardiograph automatically print, on the ECGs of patients presenting to emergency departments, TPI predictions of the benefit of thrombolytic therapy for AMI. Although the intervention had minimal effect in patient groups with already-high rates of reperfusion, it increased and expedited use of thrombolytic and overall reperfusion therapy for patients typically treated less often or less quickly. In patients with inferior AMI, the TPI significantly increased rates of use of thrombolytic therapy, use of thrombolytic therapy within 1 hour of arrival at the emergency department, and use of overall acute reperfusion (thrombolytic therapy or primary PTCA), all by 11% to 12% (Table 2). It seems that the

TPI helped physicians recognize the need for reperfusion in patients with inferior AMIs; this is the most common location of AMI, although less typically targeted for reperfusion (29). For both inferior and anterior AMIs, we confirmed earlier findings (18, 20) that women receive reperfusion less often than men. This difference was corrected when the TPI was used. The lower baseline proportions of women receiving thrombolytic therapy, receiving thrombolytic therapy within 1 hour, and receiving any reperfusion increased by 18% to 22% (Table 3). This suggests that the TPI was particularly useful for patients whose need for reperfusion is currently less well recognized.

The TPI also increased use and promptness of reperfusion in situations with logistic impediments to treatment. Delays in use of thrombolytic therapy occur when consultation with an off-site physician is needed (20, 30); the TPI's effect was pronounced in this setting. Among all patients with AMI in this situation, the TPI increased rates of use of thrombolytic therapy, use of thrombolytic therapy within 1 hour, and use of overall acute reperfusion, all by 30% to 34% (Table 4). This was underscored by even larger increases (44% to 53%) among patients seen at hospitals without on-site emergency department physicians (Table 5). These results suggest that use of the TPI in emergency departments where off-site physician consultation is needed, and possibly in EMS settings where physician supervision is entirely remote, should increase the use and timeliness of reperfusion. Given the prevalence of these settings across the United States, this could have a substantial nationwide effect on the treatment of AMI.

Many programs have been developed to increase use of thrombolytic and reperfusion therapy for AMI (3, 7–16), but individual patient-specific approaches have not previously been used. Currently, to make a decision about reperfusion in practice, physicians must recall results from controlled clinical trials that apply to general classes of patients (for example, early vs. late presentation, anterior vs. inferior AMI, large vs. small AMI, and younger vs. older patients) obtained from medical journals, pharmaceutical representatives, colleagues, and guidelines. In contrast, the TPI gives the physician specific predictions of the effect of thrombolytic therapy based on a particular patient's presenting features; vital signs; time since symptom

**Table 4. Effect of the Thrombolytic Predictive Instrument on Patients with Acute Myocardial Infarction for Whom Physician Consultation Was Entirely by Telephone (n = 271)\***

Treatment Received	Control Group (n = 146), %	TPI Group (n = 125), %	Relative Risk with TPI (95% CI)	P Value
Thrombolytic therapy within 1 hour	41.1	53.6	1.3 (1.01–1.7)	0.04
Thrombolytic therapy	47.3	63.2	1.3 (1.2–3.1)	0.01
Thrombolytic therapy or PTCA	50.7	66.4	1.3 (1.1–1.6)	0.01

\* PTCA = primary percutaneous transluminal coronary angioplasty; TPI = Thrombolytic Predictive Instrument.

onset; and detailed ECG indices of AMI earliness (in relation to the infarction process), location, and size (5, 6, 31, 32). These predictions apply the results of the many clinical trials on which the TPI models are based to specific patients. These predictions, generated when the TPI program detects ST-segment elevation consistent with AMI, seem to supplement (but not replace) physicians' decision making about treatment for specific patients.

General and patient-specific approaches probably both work, and they may well supplement each other. Indeed, the relatively high rates of thrombolytic and overall reperfusion therapy for patients with AMI, about 43% in our study, confirm improvements as a result of ongoing general attempts to improve use of thrombolytic therapy. However, room for improvement may still exist, as shown by use rates greater than 50% in Europe (33) and the fact that some groups, particularly women (17, 18, 20, 33, 34) and patients with inferior AMI (35), still seem to be undertreated. The TPI's improved rates of reperfusion among women and patients with inferior AMI suggest that additional improvement results from real-time, patient-specific support for decision making. This support also seems to help when no emergency department physician is on site or when needed consultation is available only by telephone; both situations are associated with delays in reperfusion (20, 30), and these delays are lessened with TPI use. This effect is analogous to that of the patient-specific predictions of the electrocardiograph-based acute cardiac ischemia time-insensitive predictive instrument (ACI-TIPI), which most improves emergency department triage for patients cared for by unsupervised residents and patients with stable angina pectoris, for whom improved decision making is needed (36, 37). It seems that real-time bedside support for patient-specific decision making may build on and enhance the effect of general efforts to improve care for AMI.

It is hard to project the likely effect of the TPI on

AMI-related mortality rates nationwide. Patients with small inferior AMIs have relatively low mortality rates, and increased reperfusion will therefore yield relatively small absolute benefits in survival in these patients (38). However, given that more than 60% of AMIs are inferior (34) and that the survival benefit of increased reperfusion for large inferior AMIs approaches that for anterior AMIs, the effect seen in our trial for inferior AMI should benefit many patients. In addition, improved survival rates for women, who are more likely to die of AMI, will have an important effect. Projected nationwide, the relative increases seen in our trial (10% for patients with inferior AMI and 20% for women with AMI) in rates of thrombolytic therapy, thrombolytic therapy within 1 hour, and overall reperfusion should be substantial. Additional effects can be expected from the TPI's effect on care when consultation with an off-site physician is needed or when a full-time emergency department physician is lacking; these situations are associated with longer times to reperfusion and potentially higher mortality rates (20, 30). Moreover, as prehospital thrombolytic treatment becomes more common for patients with long transport times to hospitals, the substantial effect of the TPI on rates of reperfusion in such settings, and thereby on rates of death from AMI, should increase.

It is noteworthy that when we pooled all trial settings, the TPI's effect was not seen among patients with anterior AMI and, when AMI locations were combined, among men. The need for reperfusion in patients with anterior AMIs has been emphasized longer than the need for reperfusion in patients with inferior AMIs, and anterior AMIs are more easily recognized in the precordial leads of the conventional ECG. Physicians are already skilled at identifying patients with anterior AMIs as candidates for reperfusion, and at treating them. In addition, AMI presents more "classically" and is better recognized (and treated) in

**Table 5. Effect of the Thrombolytic Predictive Instrument on Patients with Acute Myocardial Infarction Who Presented to Hospitals without an On-Site Emergency Department Physician (n = 56)\***

Treatment Received	Control Group (n = 22), %	TPI Group (n = 34), %	Relative Risk with TPI (95% CI)	P Value
Thrombolytic therapy within 1 hour	40.9	58.8	1.4 (0.8–2.6)	0.19
Thrombolytic therapy	50.0	76.5	1.5 (0.97–2.4)	0.04
Thrombolytic therapy or PTCA	54.6	79.4	1.5 (0.96–2.2)	0.05

\* PTCA = primary percutaneous transluminal coronary angioplasty; TPI = Thrombolytic Predictive Instrument.

men than women (39–41). The high rates of reperfusion for patients with anterior AMI and for men in experienced centers may require little improvement. However, although fewer than 5% of our patients were seen in hospitals without on-site emergency department physicians, and although none were treated while in transit to the hospital via EMS (when all physician input would be remote), our results show improvement in the speed and use of reperfusion among all patients with AMI (including men and those with anterior AMI) when the emergency department physician or needed physician consultants are off site. Given that many emergency departments are not staffed 24 hours per day and that, especially in rural settings, long transport times may mandate EMS use of thrombolytic therapy or early recognition for direct transport to one of the 20% of U.S. hospitals (10% of European hospitals) that can do primary PTCA (42), it seems likely that the TPI would improve care for patients with anterior AMI in such settings; this deserves further study.

The TPI-capable electrocardiographs may be particularly useful in EMS settings. Prehospital administration of thrombolytic therapy has already shown promise (43–46). The new availability of single-bolus thrombolytic therapy (47–49) and the increasing availability of 12-lead ECGs in ambulances (50–54) are providing a foundation for better exploitation of this treatment approach (55–57). Automatic generation in the field of TPI predictions for patients with ST-segment elevation indicative of AMI could support EMS use of thrombolytic therapy. In addition, for patients with contraindications to thrombolysis, prehospital identification by the TPI could obviate transport to a facility without primary PTCA ability, and therefore the need for re-transport to a PTCA-capable center. Clarifying needs and options for reperfusion in the field, especially in rural areas, would save time and thereby improve patient outcomes (58). That the TPI increased overall rates of reperfusion, by either thrombolytic therapy or primary PTCA, suggests that it could facilitate use of reperfusion in prehospital EMS settings.

As an adjunct to real-time clinical use of the TPI, retrospective use of the TPI's predictions for comparison with actual clinical outcomes may be useful in efforts to improve the care of patients with AMI. As a validated, clinically based set of predictive models, using the TPI to make risk-adjusted predictions of expected mortality rates and other outcomes might be more attractive to clinicians than the commonly used risk-adjusted predictions based on medical record review or insurance claims data (59, 60). This is supported by our confirmation of the TPI's very good predictive performance for patients receiving thrombolytic therapy or PTCA (ROC areas, 0.82 to 0.85). Because clinical improvement initiatives based on comparisons of actual and predicted clinical outcomes will succeed only to the degree that physicians accept the validity and fairness of these comparisons, use of the TPI may improve care more than current outcome reports not based on clin-

ically applicable predictive models. Accordingly, it seems reasonable to develop and test outcome reports based on the TPI.

In summary, our results suggest that the TPI is appropriate in a wide range of emergency departments and probably in prehospital EMS settings. It appears to facilitate use of thrombolytic and overall reperfusion therapy, including PTCA, and thus appears adaptive to the current trend of increasing use of PTCA. Further clinical trials should be done where the TPI might particularly benefit care, including rural and EMS settings. Also warranted are studies to understand how the TPI can best be combined with education, real-time support for decision making, and feedback reports to improve treatment of AMI.

## APPENDIX

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