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# Performance of the Thrombolysis In Myocardial Infarction Risk Index in the National Registry of Myocardial Infarction-3 and -4

## A Simple Index That Predicts Mortality in ST-Segment Elevation Myocardial Infarction

Stephen D. Wiviott, MD,*† David A. Morrow, MD, MPH,*† Paul D. Frederick, MPH, MBA,‡ Robert P. Giugliano, SM, MD,*† C. Michael Gibson, MS, MD,*§ Carolyn H. McCabe, BS,*† Christopher P. Cannon, MD,*† Elliott M. Antman, MD,*† Eugene Braunwald, MD*†

*Boston, Massachusetts; and Seattle, Washington*

**OBJECTIVES** We sought to evaluate a simple risk index based on age and vital signs in a community sample of patients with ST-segment elevation myocardial infarction (STEMI).

**BACKGROUND** A simple risk index based on age and vital signs (heart rate × [age/10]$^2$/systolic blood pressure) developed from patients with STEMI accurately predicts mortality in clinical trials of fibrinolysis. The application of such a tool in an unselected population is necessary to evaluate its utility in clinical practice.

**METHODS** To evaluate the Thrombolysis In Myocardial Infarction (TIMI) risk index for routine practice, we tested it in the National Registry of Myocardial Infarction (NRMI)-3 and -4. The risk index was evaluated as a continuous variable in patients with STEMI from NRMI and in subgroups based on age and reperfusion status.

**RESULTS** A total of 153,486 patients with STEMI were eligible. As anticipated, STEMI patients in NRMI had a higher risk index profile, as compared with those in the clinical trial (median 26.9 vs. 20, $p < 0.0001$). Classification of NRMI patients with STEMI into risk groups revealed a significant graded relationship with mortality (0.9% to 53.2%, $p_{trend} < 0.0001$, *c* statistic 0.79). The discriminatory capacity of the risk index was particularly strong in the 81,679 patients receiving reperfusion therapy (0.6% to 60%, $p_{trend} < 0.0001$, *c* statistic 0.81). For the 71,807 patients not receiving reperfusion therapy, a strong graded relationship remained (1.9% to 52.2%, $p_{trend} < 0.0001$, *c* statistic 0.71). Among the elderly, although the distribution of scores was shifted toward higher risk, the performance remained (0% to 53.1%, $p_{trend} < 0.0001$, *c* statistic 0.71).

**CONCLUSIONS** A simple risk index from baseline clinical variables routinely obtained at the first patient encounter predicted mortality in a large unselected heterogeneous group of patients with STEMI. (J Am Coll Cardiol 2004;44:783–9) © 2004 by the American College of Cardiology Foundation

Rapid and accurate risk stratification by medical and paramedical personnel is central to the initial management of patients with suspected acute coronary syndromes (1).

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Multiple tools have been developed to assist with the quantitative and qualitative assessment of risk among patients with acute coronary syndromes (2–13). These tools have been shown to predict the response to therapy (14–16).

An early in-hospital evaluation may assist with decisions regarding level of care and monitoring. Patients who are at high risk of adverse outcomes may benefit from initial triage or early transfer to tertiary care centers (17). A prehospital evaluation of patients with myocardial infarction (MI) may be strengthened by risk assessment to assist with triage decisions (18,19). A simple, generalizable, and practical risk index for the rapid evaluation of patients with MI could therefore prove valuable. Such a tool does not need to capture all available prognostic information, but should provide an accurate preliminary estimate of risk.

The risk index, calculated using the equation: (heart rate [HR] × [age/10]$^2$/systolic blood pressure [SBP]) (20), was derived from 13,253 patients enrolled in the Intravenous nPA for Treatment of Infarcting Myocardium Early (InTIME-II) trial (21), a randomized trial of lanoteplase versus alteplase as reperfusion therapy (RT) for ST-segment elevation myocardial infarction (STEMI), and validated in a second clinical trial data set (20). The risk index offered

From the *TIMI Study Group, †Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts; ‡Ovation Research, Seattle, Washington; and §Beth Israel Deaconess Medical Center, Boston, Massachusetts. The InTIME-II study was supported by Bristol-Myers-Squibb (Princeton, New Jersey); Genentech (San Francisco, California) supported the National Registry of Myocardial Infarction.

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**Abbreviations and Acronyms**

| | |
|---|---|
| CCP | = Cardiovascular Cooperative Project |
| HR | = heart rate |
| InTIME-II | = Intravenous nPA for Treatment of Infarcting Myocardium Early trial |
| IQR | = interquartile range |
| MI | = myocardial infarction |
| NRMI | = National Registry of Myocardial Infarction |
| PCI | = percutaneous coronary intervention |
| RT | = reperfusion therapy |
| SBP | = systolic blood pressure |
| STEMI | = ST-segment elevation myocardial infarction |
| TIMI | = Thrombolysis In Myocardial Infarction |

strong discrimination of mortality risk at 24 h, hospital discharge, and 30 days in the derivation set.

We sought to evaluate the performance of the Thrombolysis In Myocardial Infarction (TIMI) risk index in a real-world setting. We therefore applied the TIMI risk index to a nationally representative sample of patients presenting to U.S. hospitals with STEMI in the National Registry of Myocardial Infarction (NRMI)-3 and -4 (22,23).

## METHODS

In the present analysis, evaluation of the risk index was performed in a community-based population from NRMI-3 and -4. NRMI is an observational study of demographics, practice patterns, and health outcomes among patients with MI in the United States (22,23). Patient data from NRMI-3 (1,553 hospitals, April 1998 to June 2000) and NRMI-4 (1,272 hospitals, July 2000 to October 2002) were included. Compared with NRMI-3, patients in NRMI-4 were slightly younger, and more patients in NRMI-4 received reperfusion, had primary percutaneous coronary intervention (PCI), and had slightly less frequent history of coronary artery disease. As both sets of data represent recent practice patterns, data were combined in all analyses. All management decisions were at the discretion of the treating physician.

Patients with ST-segment elevation or presumed new left bundle branch block were classified with STEMI. Patients were further classified as having received reperfusion therapy (STEMI-RT), including fibrinolytic or primary PCI. To test for a difference in the performance of the index among those who received reperfusion, a logistic regression model was created with terms for the risk index, reperfusion status, and the interaction of these two variables. As in the InTIME-II trial, patients with complete data and a HR between 50 and 150 beats/min were included. Among nontransfer patients with STEMI, 81% were eligible (8.4% were excluded for a nondiagnostic electrocardiogram, 4.9% for HR $<50$ or $>150$ beats/min, 1.9% for cardiogenic shock, and 1.7% for missing SBP, HR, or age).

The risk index was modeled as a continuous variable, and 10-point ranges are presented for reference. The prognostic discriminatory capacity of the risk index was expressed as the *c* statistic, representing the area under the receiver operator characteristics curve for prediction of in-hospital death (24). Differences in event rates across risk index ranges were assessed using the chi-square test for trend. To further evaluate the generalizability of the risk index, each component of the risk index was examined individually and in combination in both the InTIME-II trial and the NRMI, using logistic regression. A two-tailed p value $<0.05$ was considered significant. Statistical analyses were performed using SAS version 8.02 (SAS Institute, Cary, North Carolina).

## RESULTS

A total of 153,486 patients with STEMI were included. As expected, patients from NRMI were more likely to be older and female and have a history of congestive heart failure, MI or revascularization, renal failure, and cerebrovascular accident, but less likely to be smokers, than those in the clinical trial (InTIME-II) (Table 1). Of patients with STEMI in NRMI, 81,679 patients (53%) received early RT, with 42,239 (52% of these) treated with fibrinolytics and 39,440 (48%) receiving primary PCI. There was an inverse relationship between the risk index and the proportion of patients receiving RT, with 78% of patients with a risk index of 0 to 10, 44% of patients with an index of 30 to 40, and 12% of patients with an index $>80$ treated with early RT. The baseline characteristics of the patients in NRMI who received early RT were similar to those of the InTIME-II trial patients (Table 1). Compared with patients in NRMI receiving RT (STEMI-RT), the patients who did not (STEMI–no RT) were older, more often female, diabetic, and hypertensive, and more likely to have a history of renal failure, congestive heart failure, MI, coronary artery bypass grafting, and stroke. Patients managed without RT were more also more likely to have an anterior MI.

Overall in-hospital mortality was higher in NRMI patients with STEMI (12.3%) than in the InTIME-II patients (5.4%). This difference was less pronounced for patients with STEMI in NRMI treated with RT (6.6%) as compared with those who were managed without RT (18.7%).

There were different risk index distributions among the study groups (Fig. 1). The clinical trial had a median of 20 (interquartile range [IQR] 14 to 27). The median risk index was higher in the registry patients (26.9 [IQR 17.5 to 40.4]), especially those who did not receive immediate RT (36.1 [IQR 24.5 to 50]) and the elderly (37.1 [IQR 28.2 to 49.3]). In addition to higher median risks, the patients who did not receive RT were more likely to be in the highest risk groups, with 42% of patients having an index $>40$, compared with 11% of patients who received early RT. How-

**Table 1.** Baseline Characteristics

| | NRMI | | | |
|---|---|---|---|---|
| | **InTIME-II (N = 13,253)** | **STEMI (N = 153,486)** | **STEMI–RT (N = 81,679)** | **STEMI–No RT (N = 71,807)** |
| Age (yrs) | 61 ± 12 | 67.6 ± 14.7 | 62.5 ± 13.4 | 73.6 ± 13.9 |
| ≥65 (%) | 41.9 | 58.2 | 43.4 | 75.2 |
| ≥75 (%) | 13.4 | 36.4 | 21.2 | 53.7 |
| Female (%) | 24.8 | 39.6 | 31.5 | 48.8 |
| Weight (kg) | 78 ± 14 | 79.7 ± 20.3 | 83.5 ± 19.5 | 75.1 ± 20.3 |
| Smoker | 45 | 29.3 | 38.2 | 19.1 |
| Diabetes | 14.1 | 26.2 | 20.1 | 33.1 |
| Hypertension | 30.4 | 54.5 | 49.3 | 60.4 |
| Renal failure | 1.0 | 7.0 | 2.6 | 12.0 |
| History of CHF | 3.1 | 13.8 | 4.4 | 24.4 |
| History of CVA | 0.4 | 9.1 | 4.5 | 14.4 |
| MI | 16 | 21.5 | 17.0 | 26.6 |
| Angina | 21.6 | 10.1 | 8.3 | 12.2 |
| PCI | 4.4 | 10.1 | 11.8 | 8.2 |
| CABG | 2.7 | 9.8 | 6.8 | 13.2 |
| Anterior/LBBB | 42.7 | 46.0 | 37.6 | 55.4 |
| Inferior | 57.3 | 46.2 | 58.6 | 32.2 |
| Heart rate (beats/min) | 76 ± 18 | 85.8 ± 21.2 | 80 ± 18.6 | 92.5 ± 22 |
| SBP (mm Hg) | 139 ± 22 | 141.2 ± 31.5 | 141.3 ± 80.1 | 141.2 ± 33 |
| Median TIMI risk score (25–75) (STEMI) | 3 (1–4) | 3 (1–5) | 2.5 (1–4) | 5 (3–6) |
| Median TRI (25–75) | 20.0 (14–27) | 26.9 (17.5–40.4) | 21.1 (14.7–30.3) | 36.1 (24.5–50.0) |

Data are presented as the mean value ± SD, percentage of subjects, or median value (interquartile range).

CABG = coronary artery bypass grafting; CHF = congestive heart failure; CVA = cerebrovascular accident; InTIMI-II = Intravenous nPA for Treatment of Infarcting Myocardium Early trial; LBBB = left bundle branch block; MI = myocardial infarction; NRMI = National Registry of Myocardial Infarction; PCI = percutaneous coronary intervention; RT = reperfusion therapy; SBP = systolic blood pressure; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction; TRI = TIMI risk index.

ever, among NRMI patients who did receive RT (21 [IQR 14.7 to 30.3]), the median value and distribution were similar to those in the InTIME-II trial (Fig. 1).

Among patients with STEMI treated with RT, the risk index revealed a strong graded relationship with in-hospital mortality (0.6% to 60%) across the risk index categories ($p_{trend} < 0.0001$, *c* statistic 0.81) (Table 2). The observed in-hospital mortality in each of the risk index groups was

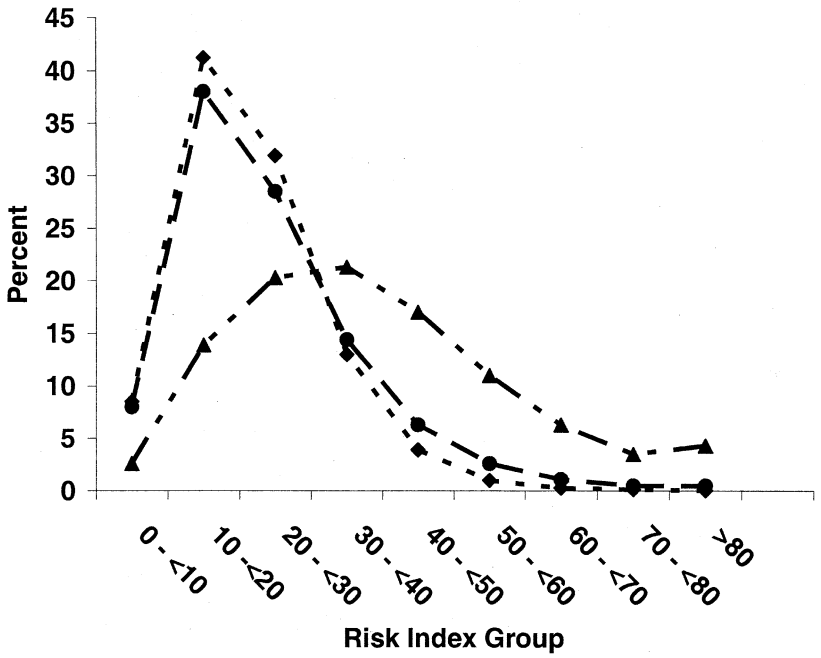


**Figure 1.** Distribution of patients (%) in risk score categories. **Lines with diamonds** = Intravenous nPA for Treatment of Infarcting Myocardium Early (InTIME-II) trial; **lines with circles** = ST-segment elevation myocardial infarction (STEMI)-reperfusion therapy (RT); and **lines with triangles** = STEMI–no RT.

**Table 2.** Relationship Between TIMI Risk Index and In-Hospital Mortality (%)

| Risk Index | InTIME (n = 13,253) | STEMI (n = 153,486) | STEMI–RT (n = 81,679) | STEMI–No RT (n = 71,807) | STEMI >65 yrs of age (n = 89,385) |
|---|---|---|---|---|---|
| 0 to <10 | 0.2 | 0.9 | 0.6 | 1.9 | 0.0 |
| 10 to <20 | 1.6 | 2.2 | 1.5 | 4.5 | 4.3 |
| 20 to <30 | 5.8 | 7.1 | 5.0 | 10.4 | 7.7 |
| 30 to <40 | 11.9 | 14.3 | 11.3 | 16.6 | 13.6 |
| 40 to <50 | 22.0 | 20.8 | 18.9 | 21.6 | 20.3 |
| 50 to <60 | 27.9 | 28.3 | 27.5 | 28.4 | 27.9 |
| 60 to <70 | 36.4 | 33.9 | 37.9 | 33.1 | 33.7 |
| 70 to <80 | 42.1 | 39.8 | 45.4 | 38.8 | 39.5 |
| >80 | 66.7 | 53.2 | 60 | 52.2 | 53.1 |
| p value | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |
| *c* statistic | 0.79 | 0.79 | 0.81 | 0.71 | 0.71 |

Abbreviations as in Table 1.

highly concordant between NRMI and the InTIME-II trial (Fig. 2). The observed mortality rates in STEMI patients from NRMI treated without immediate RT (Table 2) were higher than those in patients treated with reperfusion in NRMI ($p_{interaction} < 0.0001$). Nevertheless, the risk index maintained a significant graded association with in-hospital mortality (1.9% to 52.2%, $p_{trend} < 0.001$, *c* statistic 0.71). In the elderly, there was also a strong graded relationship with in-hospital mortality (0% to 53.1%) across risk index groups ($p_{trend} < 0.0001$, *c* statistic 0.71) (Table 2).

Evaluation of the individual components of the risk index using logistic regression showed similar associations with mortality in NRMI and the InTIME-II trial (Table 3), further supporting the assertion that the these variables are useful alone or in combination for risk stratification in a general population with STEMI.

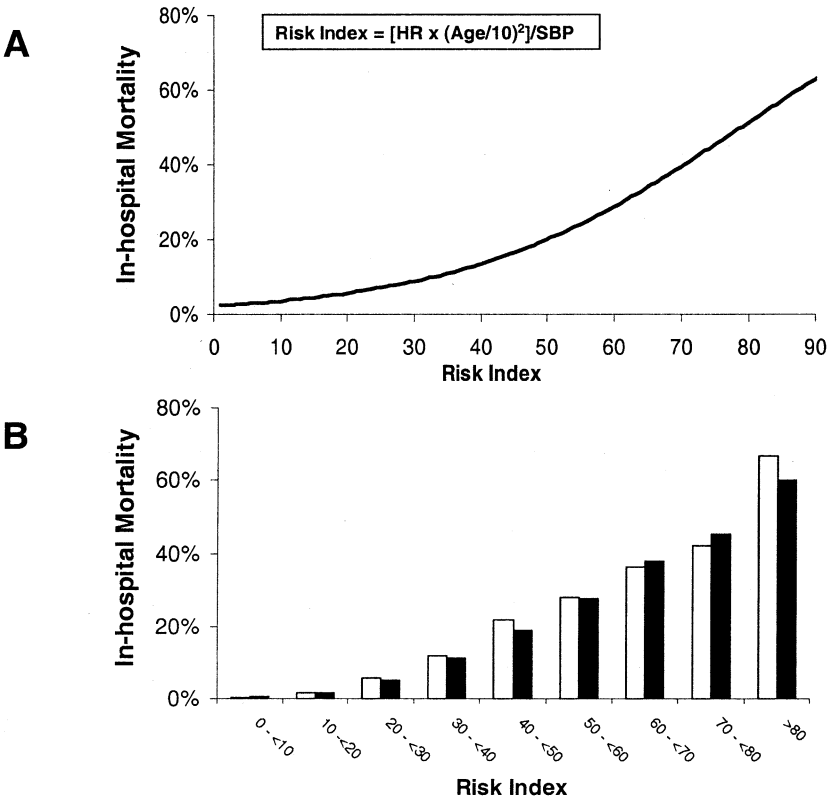


**Figure 2. (A)** Mortality (%) versus risk index in National Registry of Myocardial Infarction (NRMI) patients with ST-segment elevation myocardial infarction (STEMI). HR = heart rate; SBP = systolic blood pressure. **(B)** Risk index categories versus mortality in Intravenous nPA for Treatment of Infarcting Myocardium Early (InTIME-II) trial **(open bars)** versus NRMI STEMI-reperfusion therapy **(solid bars)**.

**Table 3.** Odds Ratios for Mortality and Discriminative Capacity (*c* Statistic) for Individual Components of the Risk Index and for the Index as a Continuous Variable

| | In TIME-II | | NRMI | |
|---|---|---|---|---|
| | OR | *c* Statistic | OR | *c* Statistic |
| Age (10 yrs) | 2.3 | 0.75 | 1.8 | 0.72 |
| BP (10 mm Hg) | 0.89 | 0.56 | 0.82 | 0.66 |
| HR (10 beats/min) | 1.3 | 0.63 | 1.2 | 0.62 |
| Index (10 U) | 2.2 | 0.79 | 2.3 | 0.79 |

BP = blood pressure; HR = heart rate; OR = odds ratio; other abbreviations as in Table 1.

## DISCUSSION

We applied a simple risk index derived in a clinical trial of fibrinolytic therapy to a large, nationally representative database of patients with MI. As a categorical indicator, this index maintained a strong graded relationship with mortality in this unselected population with MI representative of clinical practice. Based on previous experience with risk assessment in large databases, it is not surprising that the discriminatory capacity of the risk index was strongest in patients treated with RT (25). We have previously identified other factors such as medical co-morbidities that add to the risk assessment among those treated without RT (25).

**Performance of the risk index in NRMI.** Multiple classification schemes have been developed and validated for the purpose of risk stratification among patients with MI (2–8,10,13,20). Efforts have incorporated physiologic, laboratory, and demographic data into integrative risk scores, including the TIMI risk scores for STEMI (8), unstable angina/non–ST-segment elevation MI (10), the PREDICT score (4), and models derived from the Global Utilization of Streptokinase and TPA for Occluded arteries (GUSTO) trial (6,7) and Platelet IIb/IIIa Underpinning the Receptor for Suppression of Unstable Ischemia Trial (PURSUIT) (12).

In some cases, application of these tools requires detailed medical evaluation, testing, and expertise to assess hemodynamic, demographic, and laboratory features. Models that include presenting data, specific laboratory testing, and co-morbid illness are expected to have an increased discriminatory capacity (26). However, these models may not be practical for use in all situations, including initial in-hospital assessment or prehospital triage. The TIMI risk index has the advantage that it retains much of the predictive capacity of more complex systems, but can also be applied by both medical and paramedical personnel with a minimum of demographic (age) and physiologic information (HR and SBP). Additional data, including laboratory studies and physical examination, may be used later to update and refine this initial risk assessment.

This index was initially derived and validated from clinical trial data (20). Patients who are enrolled in clinical trials may have important differences from patients who are either ineligible or not enrolled (27,28). These differences result in greater heterogeneity among patients in clinical practice than among subjects in clinical trials. As would be expected, there was a greater range of risk index values seen among the NRMI participants than among subjects in the InTIME-II trial. For this reason, the risk index has been updated in this analysis, using the index as a continuous variable with a nomogram to estimate risk in clinical practice (Table 2). This updated version of the index continues to perform well in the clinical trial population and has an expanded range to better capture the range of patients in a clinical population. Nonparticipants in clinical trials tend to be at higher risk of adverse outcomes than participants. Our analysis from NRMI supports this important observation. Specifically, patients in NRMI database were more likely to experience in-hospital death than those enrolled in the InTIME-II trial (12.3% vs. 5.4%). However, when stratified by baseline risk, mortality rates were remarkably similar between patients enrolled in the clinical trial and those receiving RT in the community registry (Fig. 2). The strong discriminatory performance and excellent calibration of the index among patients treated with reperfusion in NRMI indicate that it is likely to be useful in a "real-world" population. In patients managed without RT, the risk index maintains reasonable discriminatory performance (*c* statistic 0.71); however, the event rates are higher than observed in patients receiving RT. This difference has been observed previously in the assessment of other risk prediction rules and appears to be related to the therapeutic impact of RT, as well as the effects of co-morbidities that impact eligibility for RT (25).

A previous analysis of this index using data from the Cardiovascular Cooperative Project (CCP) suggested that it did not perform as well from a discriminatory perspective in a population of elderly patients (29). However, when modeled as a continuous variable (which helps to minimize the inherent restriction introduced by including only elderly patients) in CCP, the index performed reasonably well (*c* statistic 0.71) (29), as observed in our present analysis. In addition, the index revealed a significant graded relationship with mortality across the risk groups.

Important differences exist between the populations studied (CCP, NRMI, InTIME-II), which may help to explain some of the dissimilarity between these analyses. In CCP, patients were restricted to those over age 65 years. As a result, the population was a considerably older population (median age 76 years), as compared with the InTIME-II trial (median age 61 years) or NRMI (67.6 years). In addition, a minority of patients (36%) in the CCP analysis received RT—significantly less than either the InTIME-II trial or the nationally representative NRMI (56%). Our analysis from the large NRMI registry addresses these two important issues. Second, stratified by the use of RT, there was, in fact, strong concordance between the observed event rates in the elderly versus the general population across each risk index group. Although the discriminatory capacity of the risk index was modestly attenuated in the elderly, it is

not surprising that a three-component risk score with one of the variables limited to the highest range performed less well in discriminating among this specific subgroup than among the entire population in NRMI. We believe that this limitation is acceptable in the context of using the simple risk index as a tool for the initial rapid categorization of risk, to be followed by updated risk assessment as additional information becomes available.

Finally, there were differences in design between our study and the CCP analysis. The CCP is a retrospective analysis of charts of patients identified with MI by the International Classification of Diseases-Ninth Revision-Clinical Modification codes (1994 to 1996). Data abstracted from billing records may misidentify patients with MI, and retrospective chart analysis is limited by what is available in a medical chart, compared with prospective identification of information, as performed in a clinical trial (InTIME-II), as well as the identification of patients by medical professionals and the recording of information either during or after hospitalization in a registry (NRMI).

An interesting observation from the application of the TIMI risk index to NRMI population was the striking differences in the proportion of patients receiving RT. Patients in the higher risk index groups (>40) were only 40% as likely to receive RT as those in the lower risk groups. There are likely multiple factors that explain this discrepancy, including medical co-morbidities and patient preference. We have observed previously that patients in NRMI who did not receive RT were more likely to have multiorgan failure, chronic renal failure, uncertainty regarding the diagnosis of MI, and bleeding risk (25). These factors partly accounted for the higher mortality among patients who did not receive RT. In the present analysis, performance of the risk index is also compared between the InTIME-II trial and the NRMI. It is expected that these same factors contribute to the higher mortality observed in patients in NRMI treated without RT. However, it is noteworthy that it is this group with the highest mortality that may derive the greatest absolute benefit from reperfusion, yet receive it the least.

**Study limitations.** The strengths of this analysis are the large number of patients and that NRMI reflects varying practice patterns in the U.S. The level of detail of reporting co-morbid illness in this very large database is, by necessity, less than that available in a smaller clinical trial or in clinical practice. The TIMI risk index was designed to provide a preliminary risk assessment during the first patient encounter. It does not integrate the effects of treatment, care setting, co-morbid illnesses (including those potentially involved in reperfusion eligibility), or baseline medications on outcome. Such information may be added to the risk assessment to update the initial evaluation. The index is based on initial inpatient data in both data sets. Although the findings of our analysis are likely generalizable to the prehospital setting, this application merits direct evaluation. The present analysis was not designed to assess the mechanism by which the index predicts mortality in these distinct patient populations. The risk index likely integrates baseline risk (age) with the hemodynamic effects of MI (HR and SBP). Additional evaluation in data sets in which more detailed information is available regarding ventricular function, the extent of coronary artery disease, and the cause of death may help to elucidate the mechanisms by which the index predicts mortality.

**Conclusions.** A simple risk index that can be calculated from age and vital signs is predictive of in-hospital mortality in a diverse group of patients presenting to U.S. hospitals with MI. This risk index could be used as a practical tool to rapidly risk-stratify patients with MI and could be applied by paramedical personnel in the prehospital setting or at the time of hospital presentation. Additional research to focus on the interaction between the TIMI risk index and treatment response in STEMI could advance the utility of this measure.

**Reprint requests and correspondence:** Dr. Stephen D. Wiviott, TIMI Study Group, Brigham and Women's Hospital, Cardiovascular Division, 75 Francis Street, Boston, Massachusetts 02115. E-mail: swiviott@partners.org.

## REFERENCES

1. Braunwald E, Antman EM, Beasley JW, et al. The ACC/AHA guideline update for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction—2002: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). Circulation 2002;106:1893–900.
2. Forrester JS, Diamond G, Chatterjee K, Swan HJ. Medical therapy of acute myocardial infarction by application of hemodynamic subsets (second of two parts). N Engl J Med 1976;295:1404–13.
3. Hillis LD, Forman S, Braunwald E, The Thrombolysis in Myocardial Infarction (TIMI) Phase II Co-Investigators. Risk stratification before thrombolytic therapy in patients with acute myocardial infarction. J Am Coll Cardiol 1990;16:313–5.
4. Jacobs Jr., DR Kroenke C, Crow R, et al. PREDICT: a simple risk score for clinical severity and long-term prognosis after hospitalization for acute myocardial infarction or unstable angina. The Minnesota heart survey. Circulation 1999;100:599–607.
5. Killip 3rd, T Kimball JT. Treatment of myocardial infarction in a coronary care unit: a two year experience with 250 patients. Am J Cardiol 1967;20:457–64.
6. Califf RM, Woodlief LH, Harrell JrFE ., et al., the GUSTO-I Investigators. Selection of thrombolytic therapy for individual patients: development of a clinical model. Am Heart J 1997;133:630–9.
7. Lee KL, Woodlief LH, Topol EJ, et al., the GUSTO-I Investigators. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction: results from an international trial of 41,021 patients. Circulation 1995;91:1659–68.
8. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation. An Intravenous nPA for Treatment of Infarcting Myocardium Early II trial substudy. Circulation 2000;102:2031–7.
9. Normand ST, Glickman ME, Sharma RG, McNeil BJ. Using admission characteristics to predict short-term mortality from myocardial infarction in elderly patients: results from the Cooperative Cardiovascular Project. JAMA 1996;275:1322–8.

10. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision-making. JAMA 2000;284:835–42.
11. Sabatine MS, Morrow DA, de Lemos JA, et al. Multimarker approach to risk stratification in non–ST-elevation acute coronary syndromes: simultaneous assessment of troponin I, C-reactive protein, and B-type natriuretic peptide. Circulation 2002;105:1760–3.
12. Boersma E, Pieper KS, Steyerberg EW, et al., The PURSUIT Investigators. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9,461 patients. Circulation 2000;101:2557–67.
13. Krumholz HM, Chen J, Chen YT, Wang Y, Radford MJ. Predicting one-year mortality among elderly survivors of hospitalization for an acute myocardial infarction: results from the Cooperative Cardiovascular Project. J Am Coll Cardiol 2001;38:453–9.
14. Budaj A, Yusuf S, Mehta SR, et al. Benefit of clopidogrel in patients with acute coronary syndromes without ST-segment elevation in various risk groups. Circulation 2002;106:1622–6.
15. Morrow DA, Antman EM, Snapinn SM, McCabe CH, Theroux P, Braunwald E. An integrated clinical approach to predicting the benefit of tirofiban in non–ST-elevation acute coronary syndromes: application of the TIMI risk score for UA/NSTEMI in PRISM-PLUS. Eur Heart J 2002;23:223–9.
16. Cannon CP, Weintraub WS, Demopoulos LA, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;344:1879–87.
17. Moon JC, Kalra PR, Coats AJ. DANAMI-2: is primary angioplasty superior to thrombolysis in acute MI when the patient has to be transferred to an invasive centre? Int J Cardiol 2002;85:199–201.
18. The pre-hospital management of acute heart attacks. Recommendations of a Task Force of the European Society of Cardiology and the European Resuscitation Council. Eur Heart J 1998;19:1140–64.
19. Brice JH, Valenzuela T, Ornato JP, et al. Optimal prehospital cardiovascular care. Prehosp Emerg Care 2001;5:65–72.
20. Morrow DA, Antman EM, Giugliano RP, et al. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: an InTIME II substudy. Lancet 2001;358:1571–5.
21. InTIME-II Investigators. Intravenous nPA for the Treatment of Infarcting Myocardium Early (InTIME-II), a double-blind comparison of single-bolus lanoteplase vs accelerated alteplase for the treatment of patients with acute myocardial infarction. Eur Heart J 2000;21:2005–13.
22. Rogers WJ, Canto JG, Lambrew CT, et al. Temporal trends in the treatment of over 1.5 million patients with myocardial infarction in the U.S. from 1990 through 1999: the National Registry of Myocardial Infarction 1, 2, and 3. J Am Coll Cardiol 2000;36:2056–63.
23. Rogers WJ, Bowlby LJ, Chandra NC, et al. Treatment of myocardial infarction in the United States (1990 to 1993): observations from the National Registry of Myocardial Infarction. Circulation 1994;90:2103–14.
24. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29–36.
25. Morrow DA, Antman EM, Parsons L, et al. Application of the TIMI risk score for ST-elevation MI in the National Registry of Myocardial Infarction 3. JAMA 2001;286:1356–9.
26. Singh M, Reeder GS, Jacobsen SJ, Weston S, Killian J, Roger VL. Scores for post-myocardial infarction risk stratification in the community. Circulation 2002;106:2309–14.
27. Cragg DR, Friedman HZ, Bonema JD, et al. Outcome of patients with acute myocardial infarction who are ineligible for thrombolytic therapy. Ann Intern Med 1991;115:173–7.
28. Jha P, Deboer D, Sykora K, Naylor CD. Characteristics and mortality outcomes of thrombolysis trial participants and nonparticipants: a population-based comparison. J Am Coll Cardiol 1996;27:1335–42.
29. Rathore SS, Weinfurt KP, Gross CP, Krumholz HM. Validity of a simple ST-elevation acute myocardial infarction risk index: are randomized trial prognostic estimates generalizable to elderly patients? Circulation 2003;107:811–6.