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TIMI Risk Index Predicts Long-term Mortality and Heart Failure in Patients with ST-Elevation Myocardial Infarction in the TIMI-II Clinical Trial

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Abstract

Background—TIMI Risk Index (TRI) is a simple bedside score that predicts 30-day mortality in ST-elevation myocardial infarction (MI) patients. We sought to evaluate whether TRI was predictive of long-term mortality and clinical events.

Methods—In the TIMI II trial, 3153 patients (mean age 57 ±10 years, 82% men) were randomized to invasive (n=1583) versus conservative (n=1570) strategy post-fibrinolysis with median follow-up of 3 years. TRI was divided into the 5 previously-specified groups. Primary endpoint was all-cause mortality. Secondary analyses included recurrent MI, congestive heart failure (CHF), and combined endpoints.

Results—When compared to Group 1, mortality in Group 5 was more than 5-fold higher (HR 5.83, p<0.0001), and was also increased in Group 4 (HR 2.80, p<0.0001) and Group 3 (HR 1.96, p=0.002) (c statistic 0.69). No difference was seen between Groups 1 and 2 (p=0.74). A similar increasing gradient effect was seen across TRI strata with Group 5 having the highest risk for CHF (HR 4.13, p<0.0001), and composite death/CHF (HR 4.35, p<0.0001) over Group 1. There was no difference in recurrent MI between the groups (p=0.22). After controlling for other risk indicators, the relationship between TRI and mortality remained significant: Group 5 (HR 4.11, p<0.0001), Group 4 (HR 2.14, p=0.0009), Group 3 (HR 1.69, p=0.02). When stratified by TRI groups, no differences in mortality or composite death/MI were found between treatment strategies.

Conclusion—The simple TRI can predict increased long-term mortality, CHF, and composite death/CHF.

Keywords

ST elevation myocardial infarction; mortality; congestive heart failure; TIMI Risk Index; prognosis

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BACKGROUND

The Thrombolysis in Myocardial Infarction (TIMI) risk index (TRI) for ST-Elevation Myocardial Infarction (STEMI) is a simple risk score designed to be used at initial presentation to predict 30-day mortality in STEMI patients treated with fibrinolytics.¹ The TRI is a continuous index derived from three readily available clinical variables and is calculated using the equation: $(\text{heart rate} \times [\text{age}/10]^2 / \text{systolic blood pressure})$. The TRI was originally developed in the Intravenous NPA for the Treatment of Infarction Myocardium Early (InTIME-II) study and validated in the TIMI 9 trial with high prognostic discriminatory capacity (c statistic 0.79) as a tool to triage STEMI patients.¹ Furthermore, the TRI was found to have even better discriminatory capacity (c statistic 0.81) for predicting in-hospital mortality when validated in the general population of STEMI patients treated with reperfusion therapy, including fibrinolytic or primary percutaneous coronary intervention (PCI).² In a single center cohort study of 710 unselected patients with acute coronary syndrome (ACS), the TRI was found to be predictive of long-term mortality (median 9.6 years) with a c statistic of 0.70 in patients with STEMI, but there were only 116 patients in the STEMI subgroup.³

The TIMI-II clinical trial was a multi-center randomized control trial in which 3339 patients with STEMI were initially treated with intravenous tissue-type plasminogen activator (tPA) and then randomized to either an invasive or conservative strategy.⁴⁻⁶ With median 3 years follow-up in the TIMI-II trial, we aimed to determine whether the TRI is predictive of long-term mortality and of recurrent myocardial infarction (MI), and/or congestive heart failure (CHF).

METHODS

Patient selection

Details of the TIMI-II trial have been previously reported.⁴ Briefly, men and women <76 years of age with ischemic chest pain lasting ≥ 30 min, with at least 1-mV ST-segment elevation in two contiguous electrocardiogram leads presenting within 4 hours of symptom onset within were treated with tPA and randomized to an invasive versus conservative treatment strategy. Exclusion criteria were notable for patients with history of cerebrovascular disease, prior percutaneous transluminal coronary angioplasty (PTCA) within the preceding 6 months, coronary artery bypass surgery, left bundle branch block, dilated cardiomyopathy, or other serious illness (such as cancer or renal or hepatic disorder). At the time of the study, PTCA consisted of balloon angioplasty.

A total of 3339 patients who were treated with tPA, heparin, and aspirin. At time of fibrinolysis, patients were randomized into one of two treatment strategies: (1) invasive strategy with routine coronary angiography performed 18 to 48 hours after fibrinolysis and revascularization with angioplasty or bypass grafting, as appropriate or (2) the conservative strategy in which angiography was performed only when there was evidence of spontaneous or exercise nuclear stress test-induced myocardial ischemia. As in the InTIME-II substudy in which the TRI was developed, patients with complete data and a heart rate between 50 and 150 beats per minute were included in our analysis (n=3153).¹ The heart rate and systolic blood pressure used for the calculation of TRI were the first recordings taken at the time of screening eligibility, as recorded in the case report form.

End points

Follow-up was collected (through a median of 3 years) as part of the original trial.⁶ Patient status was determined through clinic visits at 6 weeks and 1 year and by telephone contact at

3, 6, 18, 24, and 36 months. Commercial locator services and national death index searches were performed for patients whose vital status were unknown at the end of the study. The clinical endpoints used in this analysis were death, recurrent MI, CHF, composite death or recurrent MI, and composite death or CHF. Recurrent MI and CHF were adjudicated by a blinded Morbidity and Mortality Classification Committee.

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Statistical Analysis

Based on the prior development and validation set, the TRI was divided to 5 groups, as previously defined by Morrow, et al.: Group 1 as ≤ 12.5 , Group 2 as $> 12.5-17.5$, Group 3 as $> 17.5-22.5$, Group 4 as $> 22.5-30$, and Group 5 as > 30 .¹ Other risk indicators evaluated included, covariates pertaining to treatment at presentation included time to fibrinolytics, tPA dose of either 150 mg or 100 mg, and treatment strategy of invasive or conservative strategy as defined above. As previously established predictors of mortality in STEMI patients, we dichotomized weight into < 67 kg or ≥ 67 kg, Killip class II–IV to Killip class I,⁷ as well as prior history of beta blocker use within 1 week of admission or not, and time to fibrinolytics (dichotomized at the midpoint for inclusion, 2 hours). A lifetime history of > 100 cigarettes was considered a positive smoking history. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Nominal variables were expressed as frequency and percentages. For continuous variables, assessment of difference in mean values was made with two-sample t tests for comparison by treatment strategy and by analysis of variance (ANOVA) for comparison by TRI group. For categorical variables, assessment of difference in frequency was made with Fisher's Exact or Chi-square tests for comparison by treatment strategy and with the Mantel-Haenszel trend test for comparison by TRI group. Cumulative event rates stratified by TRI groups as well as comparison between treatment groups within strata of TRI groups were estimated using the product limit (Kaplan-Meier) methods and log-rank test. The c statistic,⁸ which is equivalent to the area under the receiver operating characteristic curve, was determined to evaluate the prognostic discriminatory capacity for predicting mortality with TRI treated as a continuous variable. Cox proportional-hazard models were used to evaluate the association of TRI and clinical endpoints. Stratified Cox regression model was used to evaluate the association of TRI with mortality, with covariates selected based on *a priori* knowledge of factors assessed in the emergency room that are known predictors of mortality. Covariates were kept in the models, regardless of significance, and the stratified Cox model was adjusted for demographics (gender, weight, race), risk factors (diabetes, hypertension), cardiovascular history (prior MI, previous angina, and peripheral vascular disease), presenting characteristics (prior beta blocker use, Killip class, anterior MI), treatment at presentation (tPA dose, invasive versus conservative strategy), and stratified by time-dependent covariates of smoking history, prior history of CHF, and time to fibrinolysis. We tested the proportional hazard assumption using time-varying covariates in all Cox regression models; no violations were observed. A two sided p-value of < 0.05 was considered to indicate statistical significance. All analyses were performed using SAS Version 9.1 (Cary, North Carolina).

RESULTS

Patient characteristics

A total of 3153 patients were included in the analysis. Overall, patients enrolled in the TIMI-II trial were predominantly white males, mean age 57 ± 10 years and were hemodynamically stable on initial presentation. The median follow-up period was 3.0 years, with up to 4.4 years

follow-up. The overall distribution of the TRI in the entire cohort is illustrated in Figure 1A, with a mean TRI of 20.2 ± 8.6 . As demonstrated in Figure 1B and Table 1, there was no significant difference in distribution between the invasive and conservative management strategy when stratified by TRI group. Table 1 depicts all the characteristics examined and demonstrated significant difference across TRI groups, with the exception of prior beta blocker use, time to fibrinolysis, tPA dose, and post-lytic strategy. As expected, a positive trend with heart rate and age and a negative trend with systolic blood pressure were seen with increasing TRI group as these variables define the TRI calculation. Additionally, increasing TRI group was associated with higher percentages of women, whites, and medical co-morbidities. Patients with higher TRI had lower body weight and less often were smokers.

Long-term clinical events as stratified by TRI

Of the 3153 patients, there were a total of 328 deaths, 331 recurrent MI, 666 CHF, 616 composite death or recurrent MI, and 850 composite death or CHF by the end of the study period. Figure 2 depicts the Kaplan-Meier estimates of the cumulative probability of death, recurrent MI, CHF, and composite death/CHF as stratified by the 5 groups of TRI; Table 2 provides the probability of events at various time points. Mortality and the composite endpoint of death/CHF were significantly increased across strata (both $p < 0.0001$), with the greatest estimated number of events occurring in the highest TRI group (Group 5, TRI > 30). TRI Group 5 had over 5-fold increase in all-cause mortality over TRI Group 1, with mortality of 25.7% vs 5.0%, respectively (hazard ratio [HR] 5.83, $p < 0.0001$). Similarly, patients in TRI Group 5 had over a 4-fold increase in risk for composite endpoints of death/CHF (50.4% vs 14.9%; HR 4.35, $p < 0.0001$) as compared to TRI Group 1. Additionally, estimates of CHF were significantly different among the groups ($p < 0.0001$) with a 4-fold increase in CHF risk in TRI Group 5 patients as compared to Group 1 (38.8% vs 11.7%; HR 4.13, $p < 0.0001$). There was no significant difference between the TRI groups with respect to recurrent MI ($p = 0.22$). Table 3 summarizes the HR of TRI groups for the clinical endpoints with significant differences between groups, with Group 1 as the reference standard. When stratified by TRI groups, there was no difference in hazard rates of either mortality or composite death/MI between invasive versus conservative strategies.

Predictive value of TRI on in-hospital and long-term mortality

The c statistic of TRI was 0.73 for predicting in-hospital mortality in TIMI-II. The in-hospital mortality rate was 4.9% (156/3153) with a median length of hospital stay of 10 days (range 0 to 117 days). When compared to Group 1, a gradient stepwise increase in incidence and risk of in-hospital mortality were seen with TRI Groups 3 to 5 but not for Group 2: Group 1—1.5% (9/573); Group 2—1.8% (14/786), HR 1.12, 95% confidence interval (CI) 0.48–2.58, $p = 0.80$; Group 3—4.2% (30/717), HR 2.44, 95% CI 1.16–5.14, $p = 0.02$; Group 4—6.7% (45/671), HR 3.59, 95% CI 1.75–7.38, $p = 0.0005$; Group 5—14.6% (58/397), HR 8.28, 95% CI 4.09–16.75, $p < 0.0001$. Mortality prediction was similar at 30 days (c statistic 0.74).

For predicting long-term mortality, the c statistic was 0.71 at 1 year and 0.69 through follow-up (median 3 years). As seen in Table 3, the unadjusted hazard ratio (HR) for mortality through the entire follow-up period was highest for Group 5 (HR 5.83, 95% CI 3.86–8.80, $p < 0.0001$), followed by Group 4 (HR 2.80, 95% CI 1.85–4.26, $p < 0.0001$), and then Group 3 (HR 1.96, 95% CI 1.27–3.03, $p = 0.002$), when compared to Group 1. These increased risks while slightly attenuated were significant in the final multivariable model (Figure 3, Appendix for table of full model), after stratification for smoking history, prior CHF, time to fibrinolysis, and adjustment for demographics, risk factors, cardiovascular history, presenting characteristics, and treatment at presentation. The adjusted HR remained highest for Group 5 (HR 4.11, $p < 0.0001$), followed by Group 4 (HR 2.14, $p = 0.0009$), and then Group 3 (HR 1.69, $p = 0.02$) when compared to Group 1. Group 2 was not associated with a higher risk of death over those

in Group 1 in both unadjusted (HR 0.92, 95% CI 0.57–1.50, $p=0.74$) and adjusted models (HR 0.79, 95% CI 0.47–1.33, $p=0.38$).

DISCUSSION

The TRI was developed and validated as a bedside tool to risk stratify STEMI patients and predict their 30-day mortality. This TIMI-II analysis found that in addition to predicting in-hospital and 30-day mortality, TRI was predictive of long-term mortality, CHF, and their composite but not of recurrent MI. This simple risk score identified more than 5-fold difference in mortality risk across the TRI categories.

Risk stratification of patient with STEMI is important for guiding clinical decisions with regards to initial triage of patients for receiving certain treatment strategies and the need for rapid transfer to a tertiary referral center. Several STEMI risk scores (TIMI Risk Score, GRACE, and dynamic modeling)^{7, 9–12} have been developed to facilitate the decision-making process and predict adverse clinical outcomes in patients treated with fibrinolytics. The TRI differs in that it is a simple risk index with only 3 variables (baseline age, heart rate, and systolic BP) that can be used at initial triage in the emergency room (or even the ambulance), without the need for clinical history, laboratory analysis, or a complex integer point scale system. Its robustness has led to its validation in not only STEMI patients^{1, 2} but to patients with all manifestations of acute coronary syndromes.^{3, 13, 14} In our study, we tested the utility of TRI on secondary endpoints of recurrent MI, CHF, and composite death/CHF. While there was no difference seen between TRI groups for recurrent MI, the other endpoints showed a stepwise increase in hazard. Interestingly, patients with highest TRI had the greatest risk for CHF and composite death/CHF after index hospitalization with a 4-fold increase in hazard as compared to the lowest TRI group. One could use TRI to identify the highest risk groups for having future CHF events and potentially treat these patients with more intensive heart failure therapy^{15, 16} or, as seen in two recent analyses, aggressive statin.^{17, 18}

Consistently, our study found a significant difference in mortality in both an increasing gradient and when comparing those with TRI >30 (TRI group 5) and those with TRI <17.5 (TRI groups 1 and 2). The initial validation study had described this gradient increase in 30-day mortality with TRI groups.¹ This study confirms that the rising trend persists beyond 3 years. Most notably, there were more than an 8-fold increase in in-hospital mortality and over a 5-fold increase in long-term mortality when comparing TRI >30 to those with TRI ≤12.5. After stratifying and controlling for multiple CV mortality risk factors (including those independent predictors in the TIMI Risk Score), this increase in long-term mortality was attenuated slightly but remained significant with a 4-fold increase in hazard between the highest and lowest TRI groups. Not surprisingly, since TRI is composed of age and admission vital signs, there was a slight decline in the c statistic for predicting mortality over longer period of follow-up. However, it remained independently predictive of mortality even after adjustment for other risk indicators, demonstrating the robustness of this simple index.

In our study, we were unable to identify a subgroup of STEMI patients using TRI who would benefit from routine invasive strategy over conservative management post-fibrinolysis. However, coronary interventions have progressed greatly since the time of this study when balloon angioplasty was used. It would be of interest to apply TRI to contemporary studies comparing primary PCI with fibrinolysis, where a mortality difference has been seen. It would also be of great interest to apply TRI in the newer trials of transfer strategies (such as TRANSFER-AMI)¹⁹ to see if it would help predict who should be transferred or who receive fibrinolysis on-site.

There are several limitations of this study that are noteworthy of mention. First, this study was conducted during the pre-stent era prior to availability of clopidogrel and glycoprotein IIb/IIIa inhibitors. This analysis was performed in patients receiving fibrinolysis and would not necessarily apply to STEMI patients treated with primary PCI. Lastly, the generalizability of the results from this study should be limited to patients similar to those in TIMI II.

In summary, TRI is predictive of not just in-hospital mortality, but also of long-term mortality post STEMI. With the exception of recurrent MI, TRI was additionally predictive of CHF, and composite death/CHF. As compared to the lowest TRI group, the highest TRI group had a greater than 5-fold increased risk of all-cause mortality and over 4-fold increase for CHF and composite death/CHF. TRI did not identify a subgroup of STEMI patients who benefited from either an invasive or conservative strategy, but it will be of interest to use TRI to evaluate subgroups to compare other treatment strategies for STEMI.

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Figure 1.
A. Distribution of TIMI Risk Index (TRI) in TIMI-II Cohort. B. Distribution of TIMI Risk Index by 5 Risk Groups in entire cohort, in those receiving invasive and conservative management.

Figure 2. Kaplan-Meier Curves of (A) Death, (B) Recurrent MI, (C) CHF, and (D) Composite Death or CHF as stratified by TIMI Risk Index Group. MI denotes myocardial infarction; and CHF, congestive heart failure.

Figure 3.

Adjusted Hazard Ratios and 95% Confidence Interval of TIMI Risk Index (TRI) Groups for Long-term Mortality. Stratified Cox-Proportional hazard model shown was stratified for smoking history, prior history of congestive heart failure, time to fibrinolysis, and adjusted for demographics (gender, weight, race), risk factors (diabetes, hypertension), cardiovascular history (prior myocardial infarction, previous angina, and peripheral vascular disease), presenting characteristics (prior beta blocker use, Killip class, anterior myocardial infarction), and treatment at presentation (tPA dose, invasive versus conservative strategy).

Table 1
Characteristics of the TIMI II study group and as stratified by TIMI Risk Index group

Characteristics	Total (n=3153)	Group 1 (n=582)	Group 2 (n=786)	Group 3 (n=717)	Group 4 (n=671)	Group 5 (n=397)	P-value
Demographics							
Age, yrs	56.6 ± 10.3	42.6 ± 6.1	52.8 ± 6.3	59.0 ± 6.3	64.0 ± 5.8	68.0 ± 5.0	<0.0001
Female gender	563 (17.9%)	32 (5.5%)	98 (12.5%)	139 (19.4%)	173 (25.8%)	121 (30.5%)	<0.0001
Weight, kg	81.4 ± 15.5	86.3 ± 15.8	83.8 ± 15.8	80.4 ± 14.6	78.2 ± 13.9	76.2 ± 15.4	<0.0001
<67 kg	499 (16.0%)	53 (9.1%)	97 (12.4%)	111 (15.7%)	127 (19.1%)	111 (28.6%)	<0.0001
White	2780 (88.2%)	496 (85.2%)	676 (86.0%)	633 (88.3%)	610 (90.9%)	365 (91.9%)	<0.0001
Risk Factors							
Smoking (>100 cigarettes)	2425 (77.1%)	513 (88.1%)	621 (79.0%)	553 (77.3%)	476 (71.2%)	262 (66.3%)	<0.0001
Diabetes	418 (13.3%)	39 (6.7%)	91 (11.6%)	94 (13.2%)	120 (17.9%)	74 (18.8%)	<0.0001
Hypertension	1200 (38.2%)	180 (30.9%)	278 (35.6%)	293 (41%)	286 (42.8%)	163 (41.4%)	<0.0001
Cardiovascular history							
Prior MI	449 (14.2%)	58 (10.0%)	104 (13.2%)	92 (12.8%)	122 (18.2%)	73 (18.4%)	<0.0001
Prior angina	1705 (54.1%)	286 (49.1%)	406 (51.7%)	393 (54.8%)	377 (56.3%)	243 (61.4%)	<0.0001
Prior CHF	89 (2.8%)	5 (0.9%)	8 (1.0%)	16 (2.2%)	33 (4.9%)	27 (6.8%)	<0.0001
Prior PVD	106 (3.4%)	9 (1.6%)	17 (2.2%)	22 (3.1%)	30 (4.5%)	28 (7.3%)	<0.0001
Presenting characteristics							
Systolic BP, mmHg	129.3 ± 21.7	137.1 ± 19.6	134.1 ± 20.8	130.4 ± 21.7	124.3 ± 19.9	114.4 ± 19.8	<0.0001
Heart rate, bpm	77.4 ± 15.1	74.6 ± 13.9	73.8 ± 14.2	75.4 ± 13.4	78.8 ± 14.0	89.6 ± 16.8	<0.0001
Prior beta blocker use	578 (18.4%)	100 (17.2%)	140 (17.9%)	145 (20.3%)	126 (18.8%)	67 (16.9%)	0.56
Killip class II – IV	329 (10.5%)	42 (7.3%)	58 (7.5%)	61 (8.6%)	79 (11.9%)	89 (22.7%)	<0.0001
Anterior MI	1665 (52.8%)	307 (52.8%)	390 (49.6%)	363 (50.6%)	368 (54.8%)	237 (59.7%)	0.01
Treatment							
Time to fibrinolysis, > 2 hr	2352 (74.6%)	434 (74.6%)	573 (72.9%)	533 (74.3%)	508 (75.7%)	304 (76.6%)	0.65
Dose, tPA							
100mg	2661 (84.4%)	490 (84.2%)	659 (83.8%)	613 (85.5%)	561 (83.6%)	337 (85%)	0.85
150mg	493 (15.6%)	92 (15.8%)	127 (16.2%)	104 (14.5%)	110 (16.4%)	60 (15%)	
Post-lytic Strategy							
Invasive	1583 (50.2%)	289 (49.7%)	399 (50.8%)	359 (50.1%)	335 (49.9%)	201 (50.6%)	0.92
Conservative	1570 (49.8%)	293 (50.3%)	387 (49.2%)	358 (49.9%)	336 (50.1%)	196 (49.4%)	

MI denotes myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; BP, blood pressure; and tPA, tissue-plasminogen activator.

Table 2
Kaplan-Meier Estimates of Clinical Events as Stratified by TIMI Risk Index Group in the TIMI II Trial

	Group 1 (n=582)	Group 2 (n=786)	Group 3 (n=717)	Group 4 (n=671)	Group 5 (n=397)	Log-rank p-value
All-cause mortality						
Patients who died—no. (%)	29 (5.0%)	37 (4.7%)	69 (9.6%)	91 (13.6%)	102 (25.7%)	
Death—no.(Probability of event)						
6 weeks	12 (2.1%)	13 (1.7%)	29 (4.1%)	44 (6.6%)	59 (14.9%)	
1 year	17 (3.0%)	24 (3.1%)	44 (6.2%)	69 (10.3%)	76 (19.2%)	<0.0001
2 years	23 (4.1%)	28 (3.6%)	58 (8.2%)	78 (11.7%)	90 (22.9%)	
3 years	28 (5.4%)	35 (4.9%)	62 (9.1%)	91 (14.5%)	97 (25.4%)	
Recurrent MI						
Patients with Recurrent MI—no. (%)	48 (8.3%)	84 (10.7%)	86 (12.0%)	74 (11.0%)	39 (9.8%)	
Recurrent MI—no. (Probability of event)						
6 weeks	22 (3.8%)	45 (5.8%)	56 (8.0%)	44 (6.8%)	22 (6.1%)	
1 year	36 (6.3%)	65 (8.4%)	76 (10.9%)	63 (9.9%)	31 (8.9%)	0.22
2 years	47 (8.4%)	76 (9.9%)	85 (12.3%)	68 (10.8%)	38 (11.1%)	
3 years	48 (8.7%)	84 (11.4%)	85 (12.3%)	72 (11.8%)	39 (11.6%)	
CHF						
Patients with CHF—no. (%)	68 (11.7%)	118 (15.0%)	138 (19.2%)	188 (28.0%)	154 (38.8%)	
Death or CHF—no. (Probability of event)						
6 weeks	64 (11.0%)	108 (13.8%)	118 (16.6%)	171 (25.8%)	136 (35.3%)	
1 year	66 (11.4%)	112 (14.3%)	131 (18.5%)	178 (26.9%)	144 (37.6%)	<0.0001
2 years	68 (11.8%)	114 (14.6%)	136 (19.3%)	185 (28.1%)	151 (39.7%)	
3 years	68 (11.8%)	116 (14.9%)	137 (19.5%)	187 (28.5%)	153 (40.6%)	
Composite Death or CHF						
Patients with Death or CHF—no. (%)	87 (14.9%)	145 (18.4%)	186 (25.9%)	232 (34.6%)	200 (50.4%)	
Death or CHF—no. (Probability of event)						
6 weeks	71 (12.2%)	117 (14.9%)	137 (19.1%)	192 (28.6%)	164 (41.3%)	
1 year	76 (13.1%)	129 (16.4%)	160 (22.3%)	215 (32.1%)	177 (44.6%)	<0.0001
2 years	82 (14.2%)	134 (17.2%)	175 (24.5%)	223 (33.3%)	191 (48.3%)	

	Group 1 (n=582)	Group 2 (n=786)	Group3 (n=717)	Group 4 (n=671)	Group 5 (n=397)	Log-rank p-value
3 years	86 (15.3%)	141 (18.3%)	179 (25.3%)	231 (34.9%)	196 (50.2%)	

MI denotes myocardial infarction; and CHF , congestive heart failure.

Table 3
Hazard Ratios and 95% Confidence Intervals of TIMI Risk Index Groups for Long-term Clinical Events

TIMI Risk Index	Mortality		CHF		Composite Death or CHF	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Group 1	1.00 (Reference)	N/A	1.00 (Reference)	N/A	1.00 (Reference)	N/A
Group 2	0.92 (0.57–1.50)	0.74	1.29 (0.96–1.74)	0.09	1.24 (0.95–1.62)	0.11
Group 3	1.96 (1.27–3.03)	0.002	1.72 (1.29–2.30)	0.0003	1.83 (1.42–2.36)	<0.0001
Group 4	2.80 (1.85–4.26)	<0.0001	2.64 (2.00–3.48)	<0.0001	2.58 (2.02–3.30)	<0.0001
Group 5	5.83 (3.86–8.80)	<0.0001	4.13 (3.11–5.50)	<0.0001	4.35 (3.38–5.59)	<0.0001

HR denotes hazard ratios; CI, confidence interval; MI, myocardial infarction; and CHF, congestive heart failure.

Appendix
Stratified* Cox-Proportional Hazard Model with Hazard Ratios and 95% Confidence Intervals of Covariates for Long-term All-Cause Mortality.

	HR (95% CI)	p value
TIMI Risk Index by Group		
Group 1	1.00 (Reference)	N/A
Group 2	0.79 (0.47–1.33)	0.38
Group 3	1.69 (1.07–2.67)	0.02
Group 4	2.14 (1.37–3.35)	0.0009
Group 5	4.11 (2.61–6.48)	<0.0001
Demographics		
Female gender	1.29 (0.96–1.73)	0.09
Weight <67 kg	1.09 (0.80–1.50)	0.58
White race	0.71 (0.51–0.98)	0.04
Risk factors		
Diabetes	1.54 (1.16–2.06)	0.003
Hypertension	1.30 (1.01–1.67)	0.04
Cardiovascular history		
Prior MI	1.79 (1.34–2.40)	<0.0001
Previous Angina	1.05 (0.81–1.35)	0.73
Peripheral vascular disease	2.04 (1.34–3.09)	0.0008
Presenting characteristics		
Prior beta blocker use	0.97 (0.72–1.31)	0.84
Killip class II–IV	1.42 (1.04–1.94)	0.03
Anterior MI	1.54 (1.20–1.96)	0.0006
Treatment at presentation		
tPA dose (150 mg vs 100 mg)	1.18 (0.88–1.59)	0.27
Treatment strategy (invasive vs conservative)	1.11 (0.88–1.40)	0.37

* Stratification by time-dependent covariates: smoking history, prior history of congestive heart failure, time to fibrinolysis > 2 hrs.

HR denotes hazard ratio; CI, confidence interval; N/A, not applicable; MI, myocardial infarction; and tPA, tissue-plasminogen activator.