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Prediction of Mortality After Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction

The CADILLAC Risk Score

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OBJECTIVES We sought to develop a simple risk score for predicting mortality after primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI).

BACKGROUND Accurate risk stratification after primary PCI is important. Previous risk scores after reperfusion therapy have incorporated clinical ± angiographic variables but have not considered baseline left ventricular function. Moreover, prior studies have not been validated against independent databases or studies.

METHODS The databases from the two largest multicenter, randomized AMI trials of primary PCI were utilized for score derivation (the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications [CADILLAC] trial, n = 2,082) and subsequent validation (the Stent-Primary Angioplasty in Myocardial Infarction [Stent-PAMI] trial, n = 900). Logistic regression and the jackknife procedure were used to select correlates of one-year mortality that were subsequently weighted and integrated into an integer scoring system.

RESULTS Seven variables selected from the initial multivariate model were weighted proportionally to their respective odds ratio for one-year mortality (age >65 years [2 points], Killip class 2/3 [3 points], baseline left ventricular ejection fraction <40% [4 points], anemia [2 points], renal insufficiency [3 points], triple-vessel disease [2 points], and post-procedural Thrombolysis In Myocardial Infarction flow grade [2 points]). Three strata of risk were defined (low risk, score 0 to 2; intermediate risk, score 3 to 5; and high risk, score ≥6) with excellent prognostic accuracy for survival in the derivation and validation sets (*c* statistics = 0.83 and 0.81 for 30-day mortality and 0.79 and 0.78 for 1-year mortality, respectively).

CONCLUSIONS In AMI patients treated with primary PCI, seven risk factors readily available at the time of intervention accurately predict short- and long-term mortality. Of note, measurement of baseline left ventricular function is the single most powerful predictor of survival and should be incorporated into risk score models. (J Am Coll Cardiol 2005;45:1397–405) © 2005 by the American College of Cardiology Foundation

The evolution and widespread adoption of primary percutaneous coronary intervention (PCI) represents a major advance in the management of acute myocardial infarction (AMI), resulting in a significant reduction in early and late mortality compared with pharmacologic reperfusion therapy (1). Nonetheless, considerable variability in survival rate after primary PCI is present and accurate risk stratification is therefore of clinical importance. Several risk scores using demographic and electrocardiographic variables have been developed from thrombolysis trials (2–5), but their applicability to the primary PCI setting is unknown. Moreover, catheter-based reperfusion offers the additional opportunity to include angiographic and left ventricular function data in the risk models, which are known to be of prognostic utility (6,7). Risk scores developed from populations treated exclusively by primary PCI, however, have either not incorporated any angiographic variables (8) or have excluded left ventricular ejection fraction (LVEF) (9), one of the most powerful prognostic determinates. Finally, validation against independent study populations is the most rigorous test of a risk score (10). A comprehensive clinical and angiographic primary angioplasty risk model subjected to strict validation has not been reported.

We therefore sought to derive a simple clinical scoring system for prediction of short- and long-term mortality after primary PCI utilizing clinical, procedural, and angiographic information available at the time of intervention (including left ventricular function) and to validate this risk score against an independent study cohort. To this end, the databases from the two largest multicenter, randomized AMI trials of primary PCI to date were utilized for score derivation (the Controlled Abciximab and Device Investigation to Lower

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Abbreviations and Acronyms

AMI	= acute myocardial infarction
CADILLAC	= Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications trial
CI	= confidence interval
LVEF	= left ventricular ejection fraction
OR	= odds ratio
PCI	= percutaneous coronary intervention
ROC	= receiver-operating characteristic
Stent-PAMI	= Stent-Primary Angioplasty in Myocardial Infarction trial

Late Angioplasty Complications [CADILLAC] trial [11], n = 2,082] and subsequent validation (the Stent-Primary Angioplasty in Myocardial Infarction [Stent-PAMI] trial [12], n = 900).

METHODS

The risk score was derived from the CADILLAC trial database, which comprises the largest and most comprehensive primary PCI database to date. In the CADILLAC trial, 2,082 patients of any age with AMI and symptoms lasting ≥30 min but ≤12 h who were not in cardiogenic shock at the time of presentation were enrolled (11). Additional major exclusion criteria included failed thrombolytic therapy (rescue PCI), the requirement for multivessel PCI during the index procedure, bleeding diatheses, cerebrovascular accident within the preceding two years, known hepatic or renal dysfunction, and the presence of serious co-morbidities with a life expectancy of less than one year. Angiographic inclusion criteria required a culprit artery with a reference diameter of 2.5 to 4.0 mm and lesion length <64 mm. After coronary arteriography and left ventriculography, patients were assigned randomly to either balloon angioplasty or stenting, each ± abciximab. Detailed clinical follow-up was obtained during hospitalization and at discharge, one month, six months, and one year.

For the validation set, the database from the Stent-PAMI trial was utilized, in which 900 eligible patients undergoing primary PCI were assigned randomly to stenting versus balloon angioplasty. The clinical and angiographic entry criteria, medications used, and procedural performance were similar between the Stent-PAMI and CADILLAC trials, except that abciximab was used in only ~5% of patients in the Stent-PAMI trial compared to ~53% in the CADILLAC trial, and the use of the MultiLink stent (Guidant, Santa Clara, California) in the CADILLAC trial compared with the heparin-coated Palmaz-Schatz stent in the Stent-PAMI trial afforded treatment of smaller vessels and longer lesions in the CADILLAC trial (12). The 30-day and 1-year mortality rates, however, were similar between the two studies.

Quantitative coronary angiography and left ventriculography. Quantitative coronary angiography and left ventriculography were performed at the same independent core angiographic laboratory (the Cardiovascular Research Foundation, New York, New York) for both studies. Antegrade blood flow in the infarct artery was graded using the Thrombolysis In Myocardial Infarction (TIMI) scale (13). LVEF was calculated by the area-length method (14), and regional wall motion was determined by the centerline chord method (15).

End points and statistical analysis. Categorical data were compared using the chi-square test. Continuous variables are presented as medians and interquartile ranges and were compared using the nonparametric Kruskal-Wallis test. Clinical outcomes are presented as Kaplan-Meier survival percentages and were compared using the log-rank test. For all analyses a two-sided $p < 0.05$ was considered statistically significant.

Baseline demographic, clinical, and angiographic parameters in the CADILLAC database were examined by univariate logistic regression analysis for their relation to one-year all-cause mortality, the primary end point for the current risk score. All variables in Table 1 were available for selection in this model. Left ventricular ejection fraction, hematocrit level, creatinine clearance, and age were dichotomized and treated as binary variables, based on previous work (6,16–18). Severe left ventricular systolic dysfunction was defined as an LVEF <0.40 (6). Based on World Health Organization criteria, anemia was defined as a baseline hematocrit level <39% for men and <36% for women (19). Creatinine clearance was calculated by the Cockcroft-Gault formula corrected for gender (20), and baseline renal insufficiency was defined as a creatinine clearance <60 ml/min (21). Significant univariate predictors of one-year mortality were subjected to a forward stepwise selection process (entry and exit criteria $p = 0.05$ and $p = 0.10$, respectively) in a sequence of "leave one out" jackknife procedures (n = 2,082). For variables selected in >85% of the samples, the odds ratio of one-year mortality rate was calculated in a final multivariate logistic regression analysis. Each of these variables was assigned a weighted score proportional to the multivariate odds ratio for one-year mortality. For the final score, three risk strata (low, intermediate, and high risk) were defined based on event rates for each individual score within the entire range resulting from the various combinations of weighted risk predictors. Event rates for each of these risk classes were calculated for the CADILLAC dataset and subsequently validated in the Stent-PAMI database. The discriminatory capacity of the model was assessed using the area under the receiver-operating characteristic (ROC) curve, and the difference between model-predicted and observed event rates (goodness-of-fit) was evaluated with the Hosmer-Lemeshow test (22) [$p > 0.10$ considered to indicate lack of deviation between the model and observed event rates (23)]. The prognostic utility of this 1-year risk score was also evaluated for all-cause mortality at 30

Table 1. Baseline Characteristics and Procedural Results in the Derivation and Validation Sets

	CADILLAC Derivation Set (n = 2,082)	Stent-PAMI Validation Set (n = 900)	p Value
Clinical features			
Age (yrs)	59.0 (51.0, 69.0)	60.1 (50.6, 69.6)	0.39
Male gender (%)	73.0	74.8	0.32
Diabetes mellitus (%)	16.6	15.1	0.33
Current smoker (%)	43.1	46.7	0.08
Hypercholesterolemia (%)	37.9	42.0	0.05
Hypertension (%)	48.1	42.1	0.003
Previous myocardial infarction (%)	13.7	11.3	0.09
Previous coronary angioplasty (%)	11.2	8.2	0.02
Previous bypass surgery (%)	1.9	1.5	0.46
History of cerebrovascular disease (%)	3.0	3.8	0.31
History of peripheral vascular disease (%)	2.7	4.0	0.08
Body mass index (kg/m^2)	27.2 (24.8, 30.4)	N/A	N/A
Killip class 2/3 (%)	10.9	6.9	0.0009
Sustained hypotension on admission* (%)	1.5	3.1	0.24
Symptom onset to balloon inflation (h)	3.97 (2.88, 6.10)	3.96 (2.92, 5.68)	0.27
Creatinine clearance (ml/min)	88.2 (66.1, 111.5)	85.4 (65.2, 108.3)	0.11
Creatinine clearance <60 ml/min (%)	18.1	19.6	0.40
Hematocrit (%)	43.0 (40, 45)	42.7 (39.5, 45.4)	0.13
Anemia (%)	12.0	14.4	0.08
Angiographic features			
Three vessel disease (%)	15.6	13.8	0.22
Infarct vessel = left anterior descending (%)	36.7	41.7	0.01
Reference vessel diameter (mm)	2.95 (2.61, 3.33)	2.88 (2.62, 3.27)	0.24
Minimal luminal diameter, pre (mm)	0.00 (0.00, 0.72)	0.00 (0.00, 0.86)	0.32
Diameter stenosis, pre (%)	100 (75, 100)	100 (70, 100)	0.26
TIMI flow grade 3, pre (%)	22.1	21.4	0.70
Baseline LVEF (%)	60.0 (47.3, 63.4)	55.7 (46.0, 61.9)	0.12
Baseline LVEF <0.40 (%)	20.5	20.5	0.99
Procedural features and outcomes			
Stent implanted (%)	56.8 (1,182/2,082)	56.4 (508/900)	0.87
Abciximab administered (%)	53.1	5.1	<0.0001
Maximal balloon diameter (mm)	3.50 (3.00, 3.50)	3.50 (3.00, 3.50)	0.04
Maximal inflation pressure (atm)	12 (9, 15)	12 (8, 16)	0.34
Minimal luminal diameter, post (mm)	2.25 (1.94, 2.60)	2.30 (2.02, 2.68)	0.001
Diameter stenosis, post (%)	23.1 (16.9, 31.3)	23.0 (17.0, 30.7)	0.94
TIMI flow grade 3, post (%)	95.6	91.1	<0.0001

*Defined in CADILLAC as systolic blood pressure <90 mm Hg for >30 min, or requiring vasopressors; defined in Stent-PAMI as systolic blood pressure <80 mm Hg for ≥60 min, requiring vasopressors or an intraaortic balloon pump.
LVEF = left ventricular ejection fraction; N/A = not available or applicable; TIMI = Thrombolysis In Myocardial Infarction.

days. The areas under the ROC curves of the CADILLAC score and previous predictive models were compared using the nonparametric method of Delong et al. (24).

RESULTS

Univariate and multivariate predictors of one-year mortality. Baseline characteristics and adverse event rates in the derivation and validation sets are shown in Tables 1 and 2, respectively. At one-year follow-up, 89 (4.3%) and 38 (4.3%) patients had died in the CADILLAC and Stent-PAMI trials, respectively. Statistically significant univariate predictors of one-year mortality in the CADILLAC trial are listed in Table 3. Of note, neither randomization to abciximab (odds ratio [OR] 0.96, 95% confidence interval [CI] 0.63 to 1.46], p = 0.83) nor stenting (OR 1.03, 95% CI 0.63 to 1.46, p = 0.88) were univariate correlates of one-year mortality. Similarly, neither the time from symptom onset to reperfusion (OR 1.02, 95% CI 0.96 to 1.09, p = 0.53) nor door to balloon time (OR 1.05, 95% CI 0.97, 1.14, p = 0.21) significantly predicted one-year mortality.

Seven predictors were selected in at least 85% of the jackknife samples by multivariate analysis as independent predictors of one-year mortality (Table 3). Using these variables, the area under the ROC curve was 0.81 with a Hosmer-Lemeshow p value of 0.22, indicating good discriminatory power and goodness-of-fit. When applied to the 30-day mortality end point, the area under the ROC curve for this model was 0.89 with a Hosmer-Lemeshow p value of 0.36. Of note, a simpler model was considered with only six variables, excluding post-PCI TIMI flow grades 0 to 2, for which the multivariate p value was 0.06. However, inclusion of post-procedural TIMI flow grades 0 to 2 flow in the one-year model resulted in a reduction of the −2 log

Table 2. Adverse Event Rates in the Derivation and Validation Sets

	CADILLAC Derivation Set (n = 2,082)	Stent-PAMI Validation Set (n = 900)	p Value
In-hospital adverse event rates			
Death (%)	1.6	2.4	0.14
Reinfarction (%)	0.2	0.4	0.46
Disabling stroke (%)	0.0	0.1	0.51
Ischemic target vessel revascularization (%)	0.0	0.1	0.13
30-day adverse event rates			
Death (%)	2.1	2.7	0.36
Reinfarction (%)	0.8	0.8	0.91
Disabling stroke (%)	0.1	0.2	0.63
Ischemic target vessel revascularization (%)	3.4	2.5	0.13
1-year adverse event rates			
Death (%)	4.3	4.3	0.99
Reinfarction (%)	2.4	2.9	0.49
Disabling stroke (%)	0.6	0.5	0.74
Ischemic target vessel revascularization (%)	13.3	16.0	0.10

likelihood statistic from 491.58 to 486.49 (p = 0.024), indicating that the presence of this variable in the final risk score improved the adequacy of the model, and thus it was retained.

Derivation and validation of the CADILLAC trial risk score: mortality prediction. The observed rates of one-year mortality according to this scoring system are shown in Figure 1. After identifying the one-year mortality rate and the number of patients for individual scores, a risk score was developed based on the sum of weighted predictors present in each case. For simplicity, three risk strata were defined (low risk, score 0 to 2, encompassing 56.5% of the patients in the CADILLAC trial; intermediate risk, score 3 to 5, 23.8% of patients; and high risk, score ≥6, 19.7% of patients). The predictive accuracy of this scoring system for one-year mortality was as precise when applied to the Stent-PAMI trial validation dataset as for the CADILLAC trial derivation dataset (Fig. 2A). Moreover, the predictive accuracy of the risk score was retained when applied to the 30-day all-cause mortality end point in both the CADILLAC and Stent-PAMI trial datasets (Fig. 2B). Sur-

Table 3. Clinical and Angiographic Predictors of One-Year Mortality in the CADILLAC Trial

	Odds Ratio	95% CI	p Value	Integer Score Assigned†
Univariate predictors				
Renal insufficiency	5.99	3.83–9.40	0.0001	—
In-hospital stroke	5.70	1.19–27.26	0.03	—
Baseline LVEF <40%	4.67	2.96–7.40	0.0001	—
Age >65 yrs	4.57	2.90–7.19	0.0001	—
Sustained hypotension on admission	4.50	1.69–12.02	0.003	—
Killip class 2/3	4.39	2.75–7.01	0.0001	—
Anemia	3.19	1.97–5.19	0.0001	—
Female gender	2.78	1.82–4.27	0.0001	—
Final TIMI flow grades 0 to 2	2.58	1.25–5.33	0.01	—
Infarct artery = left anterior descending	2.29	1.49–3.52	0.0002	—
Three vessel disease	2.21	1.37–3.57	0.001	—
Diabetes	1.95	1.17–3.28	0.01	—
Hypertension	1.62	1.05–2.50	0.03	—
Body mass index	0.89	0.84–0.94	0.0001	—
Reference vessel diameter	0.62	0.42–0.94	0.02	—
Final minimal luminal diameter	0.61	0.41–0.90	0.01	—
Smoker	0.50	0.31–0.80	0.004	—
Multivariable predictors*				
Baseline LVEF <40%	3.50	2.07–5.75	0.0001	4
Renal insufficiency	2.73	1.52–4.92	0.0008	3
Killip class 2/3	2.57	1.42–4.67	0.002	3
Final TIMI flow grades 0 to 2	2.31	0.97–5.54	0.06	2
Age >65 yrs	2.25	1.23–4.10	0.008	2
Anemia	2.24	1.24–4.05	0.007	2
Three vessel disease	2.07	1.18–3.63	0.01	2

*Selected in at least 85% of the multivariable analyses in the jackknife model. †Approximating the odds ratio.
CI = confidence interval; other abbreviations as in Table 1.

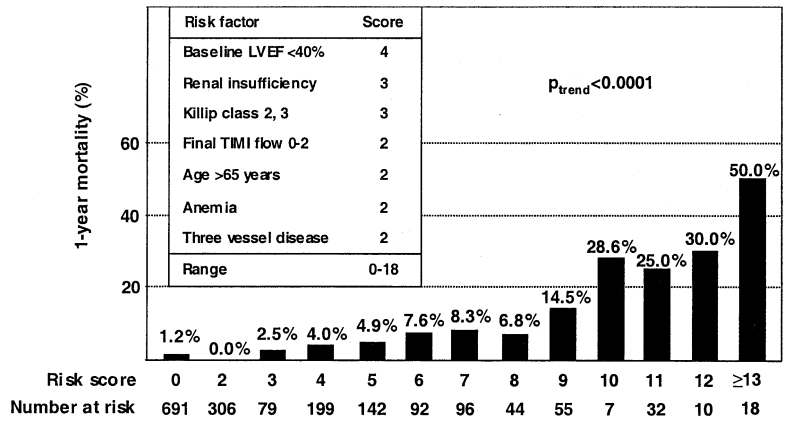

Figure 1. Integer scoring system and corresponding one-year mortality rates. LVEF = left ventricular ejection fraction; TIMI = Thrombolysis In Myocardial Infarction.

vival at various time points between 30 days and 1 year among CADILLAC patients stratified by risk class is shown in Figure 3, showing prognostic utility at all times throughout the follow-up period.

Comparison with previous score systems. To compare the performance of the CADILLAC trial score with that of previously reported models for mortality prediction after reperfusion therapy, we applied the recent TIMI ST-segment elevation (4), PAMI (8), and Zwolle (9) risk models to the validation set of the current study. As shown in Table 4, the CADILLAC trial score compared favorably with these previous risk models in prognostic performance and fitting of the data. The CADILLAC trial score was more accurate in terms of predicting 30-day mortality (p = 0.02) and 1-year mortality (p = 0.06).

DISCUSSION

The principal findings of the current study, in which a new powerful cardiac risk score was created and validated, are 1) after primary PCI in AMI, 30-day and 1-year mortality can be accurately predicted using seven clinical and angiographic variables readily available at the time of intervention; 2) baseline LVEF is the single most powerful predictive variable of mortality and should be incorporated into risk models; 3) using this prognostic score, three levels of risk strata can be created that identify patients with AMI undergoing primary PCI in whom one-year mortality is extraordinarily low (<1%), intermediate (~4% to 5%), and high (>12%); 4) the current risk score, when validated against an independent

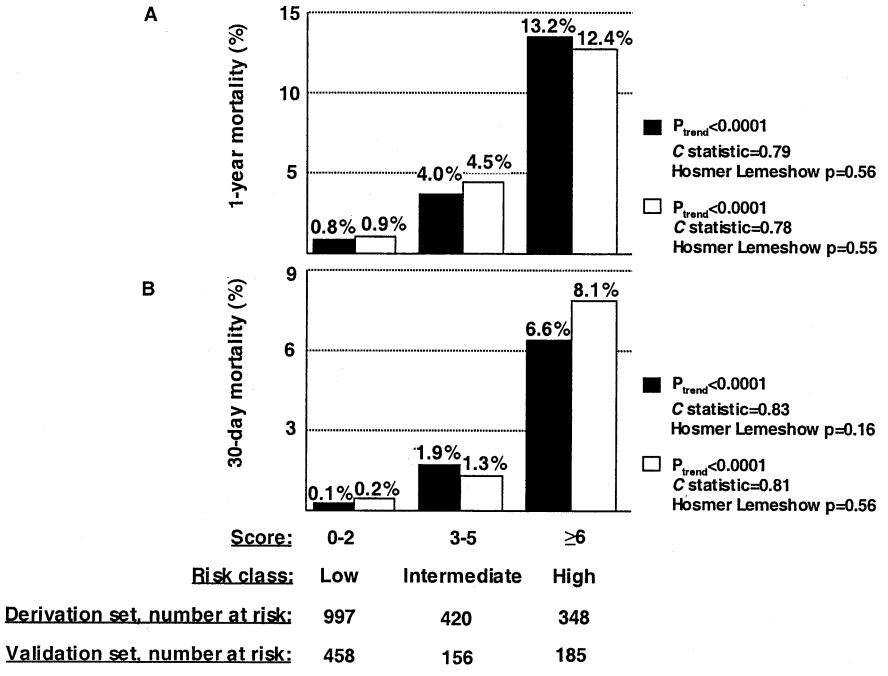

Figure 2. Score-based risk classification system with corresponding 1-year **(A)** and 30-day **(B)** mortality rates and discriminatory performance in the CADILLAC **(solid bars)** and Stent-PAMI **(open bars)** trial datasets.

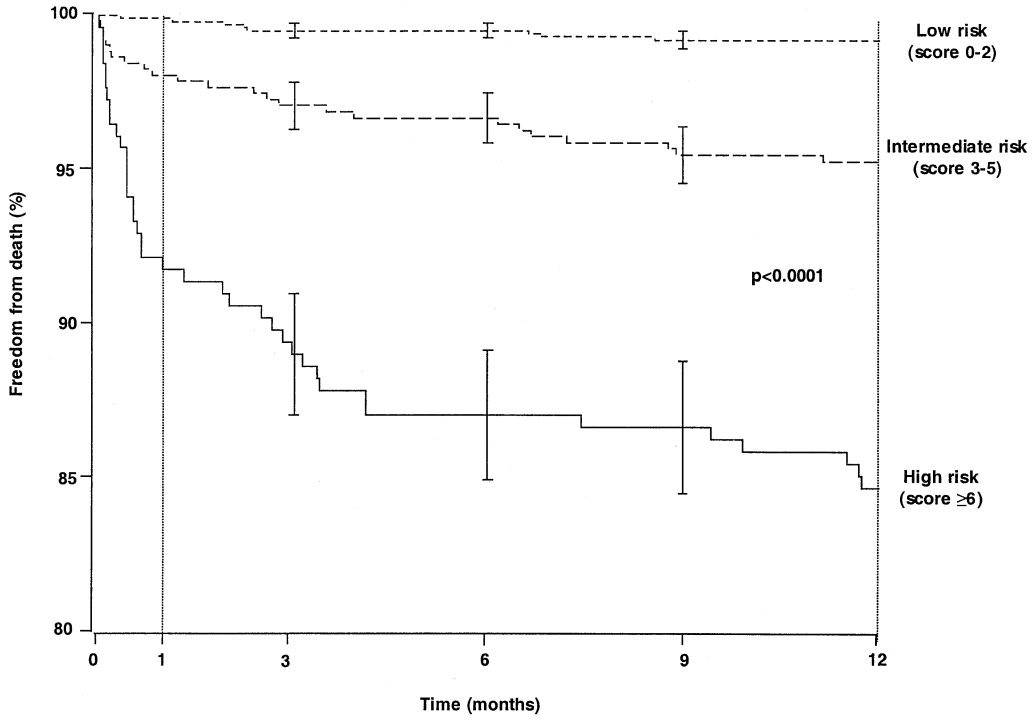

Figure 3. Freedom from all-cause mortality among the CADILLAC trial patients stratified by risk class.

randomized trial study dataset, provided more discriminatory power and goodness of fit for one-year mortality than prior risk models that did not incorporate a full range of baseline angiographic variables.

Outcome prediction after primary PCI. Accurate risk stratification after primary PCI is of importance in guiding patient management, resource utilization, and the design of clinical trials. Previous work has shown that the predictive capability of a risk model largely depends on the populations in which it was developed and to which it is applied (25). Most prior scores for mortality prediction after reperfusion therapy have been derived from thrombolytic therapy trials (2–5), whereas recent primary PCI risk models have differed from the present CADILLAC trial score in the risk factors included (8,9). Moreover, a comprehensive clinical and angiographic primary angioplasty risk model, subjected to strict validation against an independent study population, has not been reported.

The CADILLAC trial score, derived and externally validated using separate databases from the two largest multicenter randomized trials of primary PCI to date, was found to have an excellent predictive capacity for both 30-day and 1-year mortality (*c* statistics = 0.83 and 0.81 for 30-day mortality and 0.79 and 0.78 for 1-year mortality, respectively, for the CADILLAC trial derivation set and the Stent-PAMI trial validation set). Moreover, this risk score allowed the creation of risk strata in which ~56% of patients had mortality rate of <1% at 1-year (similar to that expected in an age-matched controlled population), an intermediate risk population in which ~24% of patients had 5-fold higher 1-year mortality (of ~4.0% to 4.5%), and a high risk subgroup comprising ~20% of patients with a 15-fold higher 1-year mortality (>12%). Thus, despite the fact that both trials excluded patients with cardiogenic shock, use of the risk score enables identification of a sizable cohort with a very poor long-term prognosis in whom close monitoring and aggressive therapy may be beneficial.

Predictors of mortality in the CADILLAC trial score and previous models. Angiographic findings such as LVEF and the severity of coronary artery disease are of documented prognostic importance in AMI (7) and PCI (26) risk models. Models derived from thrombolytic therapy trials in which early cardiac catheterization was not routinely performed did not incorporate these variables into the formulation of risk scores, potentially limiting their power. A secondary advantage of primary PCI as a reperfusion modality is the ability to readily assess measures of baseline left ventricular function and the extent of coronary artery disease. However, recently reported PCI risk scores have either not utilized angiographic information (8) or have excluded LVEF (9) from the candidate variables.

The current analysis calls attention to the synergistic prognostic impact of both clinical and angiographic variables as well as factors that are potentially modifiable or that mandate specific intervention. The baseline measure of LVEF was identified as the most powerful long-term determinate of mortality and should thus be incorporated into risk models to obtain maximal predictive accuracy. Patients presenting with a low LVEF should be followed up closely for signs of incipient shock that might not be apparent at presentation (27). Aggressive medical management of patients with reduced left ventricular function is warranted to prevent sudden cardiac death

Table 4. Prognostic Capability of Various Risk Scoring Systems Applied to the Stent-PAMI Validation Set

	CADILLAC Score		PAMI Score*		Zwolle Score†		TIMI Score‡	
	Area Under ROC Curve (*c* statistic)	Hosmer-Lemeshow Goodness-of-Fit (p Value)	Area Under ROC Curve (*c* statistic)	Hosmer-Lemeshow Goodness-of-Fit (p Value)	Area Under ROC Curve (*c* statistic)	Hosmer-Lemeshow Goodness-of-Fit (p Value)	Area Under ROC Curve (*c* statistic)	Hosmer-Lemeshow Goodness-of-Fit (p Value)
30-day mortality	0.81	0.56	0.78	0.42	0.74	0.16	0.70	0.06
1-year mortality	0.78	0.55	0.77	0.40	0.74	0.04	0.69	0.04

The area under the ROC curve is a measure of a score's discriminative capacity in assigning true-positive as opposed to false-positive rates for a given outcome. The Hosmer-Lemeshow test determines the difference between model-predicted event rates and observed event rates for a given outcome (goodness-of-fit is indicated by a p value >0.1) (23). *The PAMI score (8), developed from PCI-treated patients enrolled in the various PAMI trials (N = 3,252), consists of five risk categories using the following predictors: age, diabetes, Killip class, heart rate, and anterior myocardial infarction or left bundle branch block. †The Zwolle score (9) was derived from a primary PCI registry (N = 1,791). It consists of eight risk variables including: age, Killip class, anterior myocardial infarction; triple vessel disease; ischemia time; and postprocedural TIMI flow. ‡The TIMI score (4), derived from the InTIME II thrombolysis trial database (N = 15,060), utilizes 10 risk variables: age, diabetes, history of hypertension, history of angina, admission blood pressure, admission heart rate, Killip class >1; weight; anterior myocardial infarction or left bundle branch block; and time to therapy.

PCI = percutaneous coronary intervention; ROC = receiver-operating characteristic; TIMI = Thrombolysis In Myocardial Infarction.

and development of congestive heart failure (28–31). Of note, some operators do not routinely perform left ventriculography during the primary PCI procedure, and thus may not capture the full range of prognostic data available. Whether the predictive information from assessment of left ventricular function estimated by other modalities (e.g., echocardiography) or at a later time has the same prognostic utility as the LVEF obtained during baseline contrast ventriculography is unknown.

It is also worth considering intervention for other risk factors that were retained in the final multivariable model. Our findings regarding the impact of multivessel disease on survival emphasize the need for randomized clinical trials to determine whether acute multivessel intervention can improve prognosis in these high-risk patients, an approach to date not routinely recommended (32). Killip class at presentation, invariably a component of previous scores (2,4,8,9), remained an independent predictor of reduced short- and long-term survival in the current study apart from baseline LVEF and the extent of coronary artery disease, emphasizing the importance of the clinical examination for signs of mild to moderate heart failure even when left ventricular function is preserved. Anemia and renal insufficiency are recognized increasingly as conditions strongly predictive of mortality after AMI (16,17). The incremental prognostic value of these conditions was demonstrated in the current analysis and validated in an external dataset. Anemia represents a potentially modifiable risk factor, and in one report red blood cell transfusion was found to be associated with improved survival after AMI (33), an observation that warrants prospective investigation. Efforts are also warranted to minimize the occurrence of contrast nephropathy by adequate hydration and utilizing minimal amounts of low osmolar contrast (34), by consideration of n-acetylcysteine (35) and possibly alkalinization (36).

Of note, certain clinical and electrocardiographic predictors (e.g., diabetes, admission heart rate and blood pressure, electrocardiographic anterior AMI location, and/or left bundle branch block) that have been consistently present in previous scores that did not incorporate angiographic variables (2,4,5,8) are conspicuously absent from the final CADILLAC trial score. The prognostic impact of these clinical variables, which were significant correlates of survival by univariate analysis but not by multivariate analysis in this study, were likely contained within the stronger angiographic predictors of mortality in the CADILLAC trial score (e.g., LVEF at baseline, triple vessel disease). Supporting this contention is the report by De Luca et al. (9) in which consideration of multivessel disease and post-procedural TIMI flow grade excluded clinical variables other than age and Killip class from a risk model for 30-day mortality.

Study limitations. Patients presenting with cardiogenic shock, with complex coronary anatomy (e.g., left main disease or bifurcation disease, and saphenous vein graft occlusion), and those undergoing rescue PCI after failed thrombolytic therapy were excluded from the CADILLAC trial; whether these factors would add additional incremental prognostic information or result in exclusion of other

variables in the current score is unknown. Because the mortality rate in patients with cardiogenic shock remains very high even when aggressively managed by modern interventional strategies (37,38), this entity should probably be considered separately in the context of risk stratification. Operator experience and center volume (39) were not considered in the current analysis. Nonetheless, the current score was derived and validated using databases from large multicenter trials (using permissive inclusion criteria and with patients enrolled from 76 institutions in the CADILLAC trial and 62 institutions in the Stent-PAMI trial) so that it is likely to be widely applicable to a broad cross-section of patient care facilities. Measures of microvascular perfusion [e.g., resolution of ST-segment elevation and myocardial blush (40)] are absent from this as well as previous primary PCI risk score models (8,9), and may further improve prognostication beyond post-procedural TIMI flow grade. Additionally, the time from symptom onset to reperfusion was not an independent predictor of mortality in the current study. Recent data suggest that primary PCI within 3 h of symptom onset compared with longer intervals is associated with improved survival, but when the time to reperfusion exceeds 3 h, as was the case for most patients in the current analysis, further delays in reperfusion have minimal incremental effect on either early or late mortality (41). Thus, minimizing delays to PCI is always desirable, especially in patients presenting early after symptom onset. Finally, we chose to categorize the current score into only three risk classes, which likely resulted in an underestimation of the true predictive power of our model. Nevertheless, the predictive accuracy of the CADILLAC trial score compared favorably with that of previous scores that used a larger number of risk classes.

Conclusions and clinical implications. Seven clinical and angiographic parameters routinely collected and readily available at baseline or procedural completion (age, Killip class, baseline anemia and renal insufficiency, triple vessel disease, LVEF, post-procedural TIMI flow grade) accurately predict 30-day and 1-year mortality rates after primary PCI when integrated in a simple risk scoring system. Our findings indicate that in the setting of contemporary catheter-based reperfusion therapy for AMI, the severity of coronary artery disease and evaluation of baseline LVEF importantly enhance risk stratification in concert with baseline demographic and clinical profiling. Further studies are warranted to determine whether novel pharmacologic, device-based, or surgical approaches can further improve the prognosis of the patients at highest risk after primary PCI as identified by the CADILLAC risk score.

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