# Prediction of cardiovascular mortality in patients with ST-elevation myocardial infarction after primary percutaneous coronary intervention

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***Objectives*** **We analyzed a large patient group to develop a clinical risk score that could be applied to patients after primary percutaneous coronary intervention (PCI).**

***Methods*** **We reviewed 2529 consecutive patients treated with primary PCI for ST-elevation myocardial infarction between 2003 and 2008. All clinical, angiographic and follow-up data were retrospectively collected. Independent predictors of in-hospital cardiovascular mortality were determined by multivariate Cox regression analysis in all study patients.**

***Results*** **Five variables (Killip class 2/3, unsuccessful procedure, contrast-induced nephropathy, diabetes mellitus, and age >70 years) were selected from the initial multivariate model. Each of them was weighted with 1 point according to their respective odds ratio for in-hospital mortality and then total risk score was calculated for each patient with a range of 0–5 points. For simplicity, four strata of risk were defined (low risk, score 0; intermediate risk, score 1; high risk, score 2 and very high risk, score ≥ 3). Each risk strata had a strong association with in-hospital cardiovascular mortality ($P<0.001$ for trend). Moreover, among survivors after an in-hospital period, our risk score continued to be a powerful predictor of long-term mortality ($P<0.001$ for trend).**

***Conclusion*** **In patients treated with primary PCI, a risk score, which was developed from five risk factors readily available after intervention, may be useful to predict in-hospital and long-term cardiovascular mortality.** ***Coron Artery Dis*** **21:207–211 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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## Introduction

Primary percutaneous coronary intervention (PCI) has become the preferred reperfusion strategy for ST-elevation myocardial infarction (STEMI) [1]. However, clinical outcomes and survival vary greatly according to the baseline risk profile. Several risk scores using demographic and electrocardiographic variables have been developed from thrombolysis trials [2–4]; however, their applicability to the primary PCI setting is unknown. Few data are available concerning primary PCI [5,6]. A reliable simple method to predict the risk of mortality in patients after primary PCI may be valuable in selecting low-risk and high-risk patients for designing the follow-up strategy in the short and long term. Therefore, we analyzed a large group of patients develop a clinical risk score that could be applied to patients after primary PCI.

## Methods

### Patient populations

In a retrospective design, 2529 consecutive patients who underwent primary PCI for STEMI at the Institution of Siyami Ersek Thoracic and Cardiovascular Surgery Center, Training and Research Hospital between October 2003 and March 2008 were included. The study inclusion criteria were as follows: electrocardiography (ECG) revealing STEMI, defined as more than 30 min of continuous typical chest pain and ST-segment elevation of at least 2 mm in two contiguous ECG leads and/or left bundle branch block within 12 h of symptom onset or up to 18 h if there was evidence continuing ischemia or hemodynamic instability. Patients were excluded if thrombolytic agents were given for the index STEMI, if they were in cardiogenic shock, had a stroke within a month, had end-stage renal disease, or had a life expectancy from a noncardiac condition of less than 1 year. The study protocol was approved by the Siyami Ersek Thoracic and Cardiovascular Surgery Center, Training and Research Hospital's Ethics Committee.

### Analysis of patient data

The patients' demographic information, cardiovascular history and risk factors [smoking, hypercholesterolemia,

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hypertension and diabetes mellitus (DM)] were obtained from medical records. Blood values which were determined at hospital admission and on a daily basis during patient stay in hospital were recorded from medical reports. A 12-lead ECG was recorded in each patient just after hospital admission, and also MI type was recorded from ECGs.

### Coronary angiography, primary angioplasty, and stenting

All patients received chewable aspirin (300 mg) and clopidogrel (300 mg loading dose) before coronary angiography. Angiographic data of the patients were evaluated from catheter laboratory records. Emergency coronary angiography and angioplasty were performed by the percutaneous femoral approach. Heparin (10 000 IU) was administered when arterial access was secured. After visualizing the left and right coronary arteries, 2.5 mg of nitrate was selectively injected into the infarct related artery (IRA) to rule out possible coronary spasm. Angiographic assessments were made at the treating hospital by visual assessment. IRA was graded according to thrombolysis in MI classification [7]. Primary angioplasty including balloon angioplasty and/or stent implantation was performed only for IRA according to lesion type. For each procedure, interventional success at the acute phase is defined as reducing to less than 50% of obstruction and stenosis of the IRA with thrombolysis in MI 2 or 3 flow just after primary angioplasty. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/h of intravenous heparin or 1 mg/kg/day of subcutaneous low-molecular weight heparin were given; 100 mg aspirin and 75 mg clopidogrel were continued in all patients. The use was left to the discretion of the operator. Tirofiban is the only glycoprotein IIb/IIIa inhibitor used in our institution. Concomitant medical treatment with β-blockers, angiotensin converting enzyme inhibitors, and statins were prescribed according to American College of Cardiology/American Heart Association guidelines.

### Definition

Patients were evaluated according to Killip clinical examination classification [8]. Multi-vessel disease was defined as a presence of a more than 50% lesion in at least two major epicardial coronary arteries or left main coronary artery lesions. Contrast-induced nephropathy (CIN) was defined as an increase in serum creatinine level of at least 0.5 mg/dl or at least 25% from baseline within 72 h of radiocontrast administration [9]. Patient with DM was defined as the patient with documented DM using either oral hypoglycemic agents or insulin treatment at admission. Hypercholesterolemia was defined as total cholesterol of at least 200 mg/dl or use of cholesterol-lowering agents. Anemia was defined as a baseline hemoglobin concentration less than 13 mg/dl in men and less than 12 mg/dl in women.

Cardiovascular death was defined as unexplained sudden death, death owing to acute myocardial infarction, heart failure, and arrhythmia. Repeat target vessel revascularization was defined as need of PCI or coronary surgery because of restenosis or reocclusion of the IRA. Reinfarction was defined as an increase in creatine kinase (CK) – more than twice the last value associated with CK-MB at least 10% of the total CK – and ST segment reelevations.

### Follow-up

Follow-up data were obtained from hospital records or by interviewing with (directly or by telephone) patients, their families, or their personal physicians. Major adverse cardiac events (MACEs) were defined as cardiovascular death, reinfarction, repeat target vessel revascularization (percutaneous or surgical). Only cardiovascular mortality was recorded.

### Statistical analysis

Quantitative variables were expressed as mean value ± SD, and qualitative variables were expressed as percent (%). Comparison of parametric values between two groups was performed by means of two-tailed Student's *t*-test. Categorical variables were compared by the likelihood-ratio $\chi^2$ test or Fisher's exact test. The trend of in-hospital mortality, MACE, and long-term mortality according to ordinal variables was assessed by the Mantel–Haenszel $\chi^2$ for trend. Backward stepwise multivariate Cox regression analysis, which included variables with $P$ value less than 0.1 was performed to identify independent predictors of in-hospital mortality. Unsuccessful procedure, Killip class 2/3, CIN, DM, age above 70 years, anemia at admission, multi-vessel disease, female sex and tirofiban use were entered into the model. The cumulative survival curves for long-term cardiovascular mortality were constructed with the use of the Kaplan–Meier method with differences assessed with the log-rank test. A $P$ value less than 0.05 was considered statistically significant. All statistical studies were carried out with SPSS program (version 15.0, SPSS, Chicago, Illinois, USA).

## Results

### Clinical, angiographic, and procedural characteristics

The clinical characteristics of the 2529 study patients (mean age 56.4 ± 11.8, years, 2104 male, 425 female) are listed in Table 1. The prevalance of risk factors are shown in Table 1: 24.2% of the patients had DM, 40.9% had hypertension, 36.7% had hypercholesterolemia, and 62.3% were current smokers. Angiographic and procedural characteristics are also given in Table 1.

### Predictive factors for in-hospital mortality and risk scoring

In-hospital cardiac events and complications are depicted in Table 2. The overall in-hospital mortality rate was 3%. We performed univariate and multivariate analyses to

**Table 1 Clinical, angiographic, and procedural characteristics of study patients**

| | Study population ($n=2529$) |
|---|---|
| Range (years) | 26–97 |
| Age (mean) | 56.4 ± 11.8 |
| Age >70 years, *n* (%) | 369 (14.6) |
| Female sex, *n* (%) | 425 (16.8) |
| Diabetes mellitus, *n* (%) | 613 (24.2) |
| Hypertension, *n* (%) | 1035 (40.9) |
| Hypercholesterolemia, *n* (%) | 928 (36.7) |
| Current smoker, *n* (%) | 1575 (62.3) |
| PCI history, *n* (%) | 196 (7.8) |
| By-pass history, *n* (%) | 73 (2.9) |
| MI history, *n* (%) | 273 (10.8) |
| Anterior MI or LBBB | 1224 (48.4) |
| Killip class 2/3, *n* (%) | 296 (11.7) |
| Anemia at admission, *n* (%) | 624 (24.7) |
| Culprit lesion | |
| LMCA, *n* (%) | 2 (0.1) |
| LAD, *n* (%) | 1233 (48.8) |
| CX, *n* (%) | 336 (13.3) |
| RCA, *n* (%) | 936 (37) |
| By-pass graft, *n* (%) | 18 (0.7) |
| Intermediary artery, *n* (%) | 4 (0.1) |
| Single-vessel disease | 1074 (42.5) |
| Multi-vessel disease | 639 (25.3) |
| Successful procedure, *n* (%) | 2312 (91.4) |
| Tirofiban use, *n* (%) | 1243 (49.1) |
| Stent use, *n* (%) | 2149 (84.9) |
| Contrast-induced nephropathy, *n* (%) | 613 (24.2) |

CX, circumflex coronary artery; LAD, left anterior descending coronary artery; LBBB, left bundle brunch block; LMCA, left main coronary artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

**Table 2 In-hospital and long-term cardiac events and complications**

| | Study population ($n=2529$) |
|---|---|
| Time of hospital stay, days | 7.1 ± 3.9 |
| In-hospital mortality, *n* (%) | 76 (3) |
| Reinfarction, *n* (%) | 50 (2) |
| Target-vessel revascularization, *n* (%) | 111 (4.4) |
| MACE, *n* (%) | 176 (7) ($n=2407$) |
| Mortality, *n* (%) | 128 (5.3) |
| Reinfarction, *n* (%) | 230 (9.5) |
| Target-vessel revascularization, *n* (%) | 442 (18.3) |
| MACE, *n* (%) | 598 (24.8) |

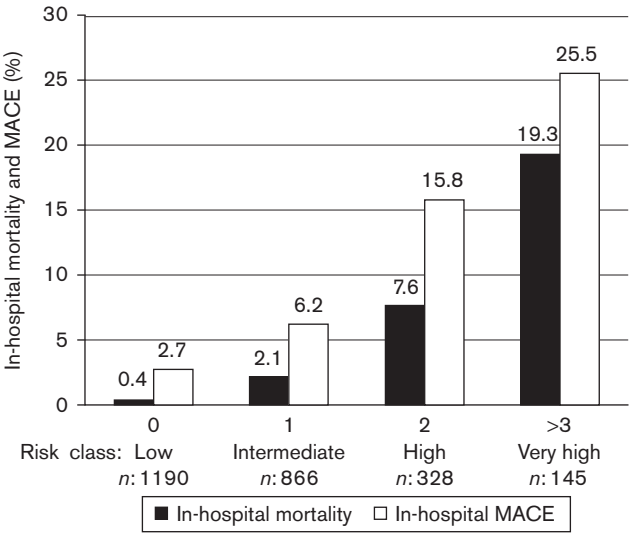
$n=2407$ for study population (there is no follow-up for 46 patients and 76 patients died during in-hospital period).
MACE, major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization).

**Table 3 Univariate and independent predictors of in-hospital mortality**

| | Odds ratio | 95% CI | *P* value | Risk score[a] |
|---|---|---|---|---|
| Univariate predictors | | | | |
| Unsuccessful procedure | 10.04 | 6.23–16.17 | <0.001 | – |
| Killip class 2/3 | 5.68 | 3.34–9.66 | <0.001 | – |
| Contrast-induced nephropathy | 4.64 | 2.73–7.9 | <0.001 | – |
| Diabetes mellitus | 4.45 | 2.71–7.32 | <0.001 | – |
| Age >70 years | 4.31 | 2.69–6.9 | <0.001 | – |
| Anemia at admission | 2.61 | 1.59–4.28 | <0.001 | – |
| Multi-vessel disease | 2.09 | 1.31–3.33 | 0.002 | – |
| Female sex | 1.68 | 0.98–2.85 | 0.055 | – |
| Tirofiban use | 0.55 | 0.33–0.89 | 0.016 | – |
| Independent predictors | | | | |
| Killip class 2/3 | 3.47 | 1.59–5.75 | <0.001 | 1 |
| Unsuccessful procedure | 3.34 | 1.63–6.66 | 0.001 | 1 |
| Contrast-induced nephropathy | 3.29 | 1.72–6.29 | <0.001 | 1 |
| Diabetes mellitus | 3.02 | 1.59–5.75 | 0.001 | 1 |
| Age >70 years | 2.93 | 1.51–5.68 | 0.001 | 1 |

CI, confidence interval.
[a]Approximating the odds ratio.

**Fig. 1**



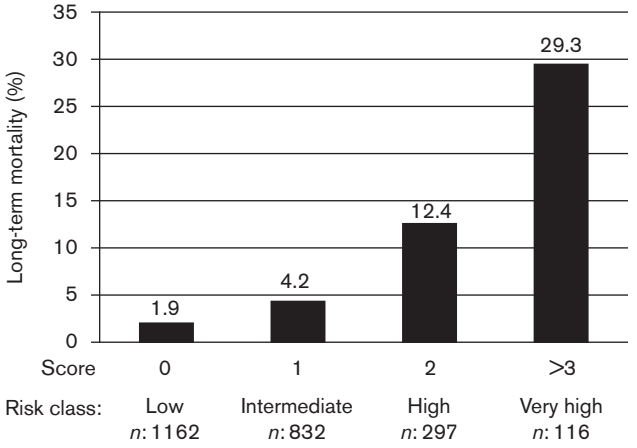

In-hospital mortality and MACE in study patients according to the risk score. MACE, major adverse cardiac events.

determine the factors that were associated with in-hospital mortality (Table 3). The following were considered independent variables: Killip class 2/3 [odds ratio (OR): 3.47, 95% confidence interval (CI): 1.59–5.75, $P < 0.001$], unsuccessful procedure (OR: 3.34, 95% CI: 1.63–6.66, $P = 0.001$), CIN (OR: 3.29, 95% CI: 1.72–6.29, $P < 0.001$), DM (OR: 3.02, 95% CI: 1.59–5.75, $P = 0.001$), age above 70 years (OR: 2.93, 95% CI: 1.51–5.68, $P = 0.001$). Using these variables as risk indicators, we developed a simple risk scoring system. The independent predictors of in-hospital mortality were assigned a risk score based on their ORs and then total risk score was calculated for each patient with a range of 0–5 points (Table 3). For simplicity, four risk class were defined (low risk, score 0; intermediate risk, score 1; high risk, score 2; and very high risk, score $\geq 3$). The in-hospital cardiovascular mortality rate, as well as in-hospital MACE rate, significantly increased with this score (Fig. 1). In addition, the risk score had highly significant relation with hospital stay in patients with score of 0 whose hospitalization averaged 6.4 ± 3 days, whereas those with a score of at least 3 stayed an average of 9.8 ± 6.3 days ($P < 0.001$ for trend).

## Long-term prognosis

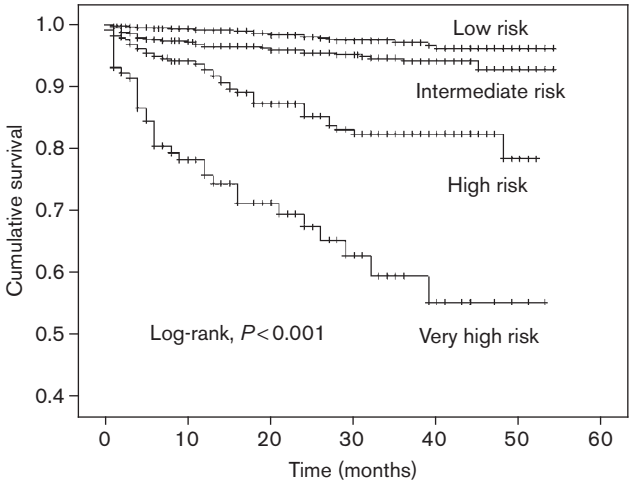
Long-term cardiac events and complications are summarized in Table 2. The median follow-up time was

**Fig. 2**




Long-term mortality among survivors of hospitalization according to the risk score.

**Fig. 3**




Kaplan–Meier survival curves for long-term cardiovascular mortality in four risk strata.

21 months. Follow-up data after discharge were not obtained for 46 (1.8%) patients. The overall long-term mortality rate for survivor patients after an in-hospital period was 5.3%. Moreover, among survivors after in-hospital period, our risk score continued to be a powerful predictor of long-term mortality ($P < 0.001$) (Fig. 2). The Kaplan–Meier survival curves for long-term cardiovascular mortality stratified by risk class are presented in Fig. 3.

## Discussion

Primary PCI is associated with a low incidence of recurrent ischemic events [10,11] and allows to make an adequate risk stratification of STEMI patients at the time of initial angiography. The second primary angioplasty in MI (PAMI-II) investigators have shown that the low-risk subsets of STEMI patients undergoing successful primary PCI can be safely discharged from the hospital on day 3 [12]. However, what defines low risk is less clear. Is it the clinical risk status or the angiographic success? We developed a simple risk score for patients who underwent primary PCI and this risk score was able to predict in-hospital and long-term outcomes.

Interestingly, the independent predictors of in-hospital cardiovascular mortality in our study have also been shown to increase mortality in different studies investigating outcome in primary PCI [13–15]. Killip class 2/3, unsuccessful procedure, CIN, DM, and age above 70 years were identical in terms of affecting mortality. Therefore, according to their OR each of them was scored with 1 point.

With regard to primary PCI, there are two important risk scores, which are the PAMI and Cadillac risk scores [5,6]. The PAMI risk score is the first predictor of mortality developed specifically from a cohort of patients treated with PCI for STEMI. Heggunje *et al.* [14] indicated unsuccessful procedure, which was also an important determinant in our study, as the prime determinant of clinical outcome in patients undergoing primary PCI. However, the PAMI risk score is a clinical score and has not incorporated any angiographic variables [5]. Patients with clinically low-risk profile are not at low risk if there is an unsuccessful PCI [14]. In our population, such as in the Cadillac risk score [6], unsuccessful procedure was an independent predictor of mortality.

Our risk score is a simple one, which incorporates both clinical and angiographic variables. It also includes CIN, which frequently complicates primary PCI, even in patients with normal renal function. We know that CIN is associated with higher in-hospital complication rate and mortality [13].

Currently, patients with a low clinical risk status are often selected for early discharge, whereas high-risk patients are observed for a longer period. Our risk score may help in defining low-risk patients. With a risk score of 0, which means none of the well-known predictors of in-hospital mortality are present, may act as a surrogate for early discharge. It may be useful to predict not only in-hospital mortality but also long-term mortality with this score. The long-term cardiovascular mortality rate (Fig. 3), as well as the in-hospital mortality, revealed a significant gradation as the risk score increased in the study population. Moreover, this risk score allowed the creation of risk strata: low-risk patients in which 48.2% of all patients including mortality rate of less than 2% at long-term, an intermediate risk population in which 34.6% of all patients including two-fold higher long-term mortality, high-risk subgroup comprising 12.3% of all patients with

a six-fold higher long-term mortality, and very high-risk population comprising 4.9% of all patients with a 15-fold higher long-term mortality. Thus, despite the fact that we 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.

In conclusion, five clinical and angiographic parameters routinely collected and readily available at baseline or procedural completion (Killip clas 2/3, unsuccessful procedure, CIN, DM, and age > 70 years) may be useful to predict in-hospital and long-term cardiovascular mortality rates after primary PCI when integrated in a simple risk scoring system.

### Study limitations

Several limitations need to be kept in mind when interpreting the results of this study. First, this study carries the well-known limitation of the retrospective design. Second, our study patients were limited only to a single center. Our findings should be confirmed and application of the risk score should be validated in a large multicenter trial.

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All authors explicitly declare that this study has no conflict of interest, any financial or other relationships.

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