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EuroHeart score for the evaluation of in-hospital mortality in patients undergoing percutaneous coronary intervention

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Aims The applicability of currently available risk prediction models for patients undergoing percutaneous coronary interventions (PCIs) is limited. We aimed to develop a model for the prediction of in-hospital mortality after PCI that is based on contemporary and representative data from a European perspective.

Methods and results Our analyses are based on the Euro Heart Survey of PCIs, which contains information on 46 064 consecutive patients who underwent PCI for different indications in 176 participating European centres during 2005–08. Patients were randomly divided into a training ($n = 23\,032$) and a validation ($n = 23\,032$) set with similar characteristics. In these sets, 339 (1.5%) and 305 (1.3%) patients died during hospitalization, respectively. On the basis of the training set, a logistic model was constructed that related 16 independent patient or lesion characteristics with mortality, including PCI indication, advanced age, haemodynamic instability, multivessel disease, and proximal LAD disease. In both the training and validation data sets, the model had a good performance in terms of discrimination (*C*-index 0.91 and 0.90, respectively) and calibration (Hosmer–Lemeshow *P*-value 0.39 and 0.18, respectively).

Conclusion In-hospital mortality in PCI patients was well predicted by a risk score that contains 16 factors. The score has strong applicability for European practices.

Keywords Percutaneous coronary intervention • Hospital mortality • Peri-procedural complications • Risk stratification • Predictive model

Introduction

Since its introduction by the late Andreas Grüntzig in 1979, percutaneous coronary interventions (PCIs) have been applied to the benefit of millions of patients across the globe. Over the years, this procedure has evolved from elective balloon angioplasty in selected centres to widely available emergency PCI with stent placement. As technology, pharmacology, and operators' experience with PCI grow, the procedure-associated risks decrease.[1] However, this intervention is still related with mortality, which varies between different groups of patients.

To identify high-risk patient groups, risk models are developed that relate patient and lesion characteristics to major complications after PCI.[2–8] Especially in situations where it is difficult to select the most appropriate treatment strategy, they can be of extra value. Risk models can then be used to systematically estimate the patient's risk of adverse events. Such estimate might then be used to help the physician decide on further patient management, as high-risk patients might be treated differently than low-risk patients.

It is broadly accepted that currently available risk prediction models for PCI patients have limited applicability, mainly because

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of heavy selection of the patients who form the model-development data set. They were either single-centre studies,[3,5,8] a selected study cohort,[2,9] or studies from an era without techniques such as drug-eluting stents; or new anti-platelet medications.[2,4,6,7] These limitations were overcome by Peterson *et al.*,[10] who developed a model based on 588 398 procedures from the American NCDR CathPCI Registry database. However, as this analysis was performed in a geographically different population, its use might be limited for a European population.[11] Additionally, the actual use of risk prediction models in routine clinical practice may be an issue. In general, one might expect that models that are based on data that are experienced as 'close' will have a good chance of being implemented. In that respect, models based on European data might more easily penetrate European practices than models based on US data.

Furthermore, several risk models did not have separate training and validation cohorts.[2,7,8,12] Without such separate cohorts, the training data cannot not be formally validated. As a consequence, their reliability remains uncertain.

The Euro Heart Survey of PCIs (EHS-PCI) was developed to obtain quantitative information on the adherence to guidelines and outcomes in European patients undergoing PCI for different indications. The survey was undertaken during 2005–08 and includes data on 46 064 patients from European hospitals. Thus, the EHS-PCI provides a unique opportunity to develop (and validate) a model for the prediction of patient prognosis after PCI, which reflects the modern clinical practice. In view of the large number and large variety of hospitals that participated in EHS-PCI, the results of this analysis will potentially be applicable to a broad variety of European practices.

Methods

PCI Registry within the Euro Heart Survey programme

The EHS programme of the European Society of Cardiology (ESC) was originally designed as a series of surveys, to obtain information on the application of clinical practice guidelines[13] in the ESC member countries, covering the broad spectrum of cardiology practice,[14] an extensive descriptive paper about which is currently being composed. Typically, patient enrolment in EHSs was scheduled for short-term periods of 3–6 months, thus taking the risk of being influenced by accidental, or just structural, season-bound variations in patient management or events. In contrast, patient enrolment in the EHS-PCI Registry lasted for a period of 3 years, from May 2005 to April 2008. That period is long enough to level off accidental situations, as well as structural differences in patient management between participating hospitals, which makes it greatly suitable for our purpose.

Patients and procedures

A total of 176 centres with PCI facilities from 33 ESC member countries participated in the EHS-PCI Registry. The sample of hospitals consisted of a mixture of tertiary referral university hospitals (48%), hospitals that could be considered satellites of university hospitals (15%), district or regional hospitals (13%), specialist cardiology centres (11%), community hospitals (8%), and private hospitals (5%).

Local investigators were asked to continuously enrol all consecutive patients undergoing emergent, urgent, or elective PCI, irrespective of any other condition. Patients who participated in (randomized) trials or other registries were eligible for inclusion. Investigators who could not warrant enrolment of each and every patient throughout the entire study period were allowed to participate if consecutive patients could be realized from Days 1 to 7 of every calendar month. We had no system installed to verify whether the principle of consecutive patient enrolment was satisfied.

Data were collected on a broad range of patient characteristics, including the clinical indication for PCI, cardiovascular risk factors, history of cardiovascular diseases, and co-morbidities. Percutaneous coronary intervention-related data were collected as well, including the number and location of significant lesions, and the ACC-AHA lesion classification.[15,16] An electronic case record form (eCRF) was used for data capture, which was programmed on the basis of the Cardiology Audit and Registration Data Standards (CARDS) for PCI.[17,18] The eCRF was accessible via the Internet for data entry and editing. Data were securely stored on a computer mainframe that was physically located in the European Heart House, Nice, France. Automated edit checks were performed to search for missing data, contradictory data entries, as well as for values that are out of the specified normal range. Additionally, manual edit checks were performed by the data management staff of the European Heart House. Final editing of the data, as well as data analyses, was performed at the Institut für Herzinfarktforschung Ludwigshafen an der Universitaet Heidelberg (IHF), Ludwigshafen, Germany. Any issues that appeared during this process were resolved in cooperation with the local investigators.

The protocol of the EHS-PCI Registry was approved by each local Ethics Committee when required. All patients provided informed consent for processing their data anonymously.

Primary objective

The EHS-PCI Registry was designed to evaluate the application of PCI-related treatment guidelines in routine clinical practice. With respect to patient outcome, the current study focuses on mortality. In this manner, endpoints that are vulnerable for observer bias, such as re-myocardial infarction (MI), are avoided and adjudication of such events is not required. All-cause mortality was reported by the local investigators and not adjudicated by a Clinical Event Committee/Data Safety Monitoring Board.

Statistical analysis

When patient characteristics were incomplete, data were imputed. Otherwise, the missing patient data might lead to biased estimates. Since occasionally not all data can be collected in patients who die early, patients with incomplete data often have a higher mortality. Missing values were imputed with the expected value according to gender, age, and PCI indication. We also performed a sensitivity analysis using multiple imputation methods. We found that all variables except prior renal failure (RF) and prior MI were of influence in all models. These two variables were included in some models but not in others (RF included in 6 of 20 models and prior MI included in 11 of 20 models). As with regression imputation the best goodness of fit was achieved, this strategy was chosen.

The percentage of missing data in variables that were significant in multivariate analyses was: 9.1% for bifurcation lesion, 8.7% for haemodynamic instability, 5.3% for valvular heart disease, 3.9% for TIMI flow, 3.4% for body mass index (BMI), and 3.2% for smoking status; other

variables had fewer than 2% missing data. Discharge status, gender, age, and PCI indication were known in all patients.

The database was randomly divided into two equal parts by using a specific application of the statistical analysis program. The first part was used to develop the mortality risk score ('training data set'). The second part was used to validate the score ('validation data set').

Univariate logistic regression analyses were applied on the training data set to study the association between a broad range of clinical and procedural characteristics (which are listed in *Table 1*) and the incidence of the primary objective. Variables that were associated with in-hospital death with a significance level of $P < 0.5$ entered the multivariate stage. A value of $P < 0.5$ was chosen in order not to miss any potential variables in the multivariate model. The final multivariable regression model was then constructed using the backward elimination of the least significant variables, until all variables had a significance level of $P < 0.15$. Subsequently, a mortality risk score was determined that included all variables that composed the final regression model. The contribution of

Table 1 Baseline characteristics of the study patients

	Training cohort	Validation cohort	*P*-value
Number of patients	23.032	23.032	
Age (years)	64 (55, 72)	64 (56, 72)	0.85
Men	74	74	0.81
Indication for PCI			
Admission with STEMI	18	17	0.14
Admission with non-STEMI	13	13	0.73
Stabilized ACS	21	21	0.56
Elective procedure	49	49	0.37
Body mass index	27 (25, 30)	27 (25, 30)	0.63
Hypertension	69	70	0.53
Hypercholesterolaemia	64	65	0.21
Diabetes mellitus	25	25	0.81
Current smoker	27	27	0.25
Ever smoker	52	52	0.53
Prior PCI	24	25	0.36
Prior CABG	6.2	6.3	0.78
Prior myocardial infarction	34	34	0.64
Congestive heart failure	11	11	0.71
Peripheral vascular disease	6.0	6.0	0.83
Prior stroke	4.1	4.1	0.74
Chronic renal insufficiency	3.5	3.5	0.89
Valvular heart disease	2.1	2.3	0.22
Number of diseased vessels			
1	47	47	0.11
2	31	32	0.02
3	21	21	0.45
Left main	4.5	4.6	0.53
Proximal LAD diseased	34	34	0.53
Bifurcation lesion	16	16	0.47
Type-C lesion	28	28	0.41
Haemodynamic instability (at presentation)	2.7	2.7	0.71
Transferred from other hospital	23	23	0.57
Left ventricular function[a]			
EF >50%	69	69	0.88
EF 41–50%	19	19	0.65
EF 31–40%	8.9	8.6	0.37
EF <30%	4.1	4.0	0.79

Continuous data are presented as median values (25th–75th percentile); dichotomous data are presented as percentages. EF, ejection fraction.
[a]Based on 32 267 patients

these variables to the risk score was weighed according to the corresponding regression coefficient in the logistic model [i.e. the natural logarithm of the corresponding odds ratio (OR)].

The performance of the mortality risk score was finally studied with respect to discrimination (*C*-index) and calibration [Hosmer–Lemeshow (H–L) goodness-of-fit test] in the training and in the validation data set.

All analyses were repeated for the cohort of patients who presented with ST-elevation MI (STEMI).

The analyses were performed with SAS 9.1 software.

Table 2 Association between baseline characteristics and in-hospital mortality in the training cohort

	In-hospital death	Crude odds ratio and 95% CI	Multivariable adjusted odds ratio 95% CI
Age, years (median)	71/64	1.05 (1.04–1.06)	
Age categorized (years)			
<50	0.73	1	—
≥50–60	0.83	1.1 (0.69–1.9)	—
≥60–70	1.2	1.7 (1.03–2.7)	1.7 (1.2–2.5)
≥70–80	2.0	2.7 (1.7–4.3)	2.4 (1.7–3.4)
≥80	4.7	6.8 (4.2–11)	4.2 (2.8–6.5)
Female	2.2/1.2	1.8 (1.5–2.3)	1.6 (1.2–2.1)
Body mass index <25	2.2/1.1	2.0 (1.6–2.5)	1.8 (1.4–2.3)
Hypertension	1.3/1.4	0.93 (0.74–1.2)	—
Hypercholesterolaemia	0.94/1.8	0.57 (0.46–0.71)	—
Diabetes mellitus	2.1/1.1	1.8 (1.4–2.2)	1.9 (1.5–2.5)
Ever smoker	1.2/1.3	0.94 (0.76–1.2)	1.4 (1.04–1.9)
Prior PCI	0.77/1.6	0.52 (0.38–0.71)	—
Prior CABG	0.85/1.4	0.63 (0.36–1.09)	0.35 (0.18–0.69)
Prior myocardial infarction	1.3/1.4	0.92 (0.73–1.2)	—
Congestive heart failure	1.5/1.4	1.1 (0.79–1.5)	—
Peripheral vascular disease	2.4/1.3	1.8 (1.3–2.6)	—
Prior stroke	3.2/1.3	2.4 (1.7–3.5)	1.8 (1.2–2.8)
Chronic renal insufficiency	3.1/1.3	2.3 (1.5–3.5)	—
Valvular heart disease	2.6/1.3	1.9 (1.1–3.4)	1.7 (0.83–3.4)
Number of diseased vessels			
1	0.85	1	—
2	1.4	1.7 (1.3–2.2)	—
3	2.9	3.5 (2.7–4.6)	1.4 (1.1–1.9)
Left main	5.3/1.3	4.2 (3.1–5.7)	2.2 (1.5–3.3)
Proximal LAD diseased	2.4/1.0	2.4 (1.9–3.0)	1.6 (1.2–2.0)
Bifurcation lesion	2.1/1.5	1.5 (1.1–1.9)	1.6 (1.1–2.1)
Type-C lesion	2.6/1.0	2.6 (2.1–3.2)	1.5 (1.2–1.9)
TIMI flow 0/1 before PCI.	3.4/0.71	4.9 (3.9–6.2)	1.5 (1.2–2.1)
Indication for PCI			
Elective procedure	0.24	1	—
Stabilized after ACS	0.86	3.6 (2.1–6.2)	2.6 (1.5–4.4)
Admission with non-STEMI	2.1	9.1 (5.9–14)	5.0 (3.2–7.8)
Admission with STEMI	5.4	24 (16–35)	7.8 (5.1–12)
Haemodynamic instability	29/0.83	52 (41–66)	17 (13–23)
Left ventricular function[a]			
Class I (>50%)	0.46	1	—
Class II (31–50%)	2.1	4.6 (3.2–6.4)	—
Class III (≤30%)	11.5	28 (19–40)	—

Continuous data (age) are presented as median values; dichotomous data are presented as percentages. For in-hospital mortality, data represent mortality when variable is present (first number) or absent (second number). Left ventricular function was not used for multivariate analysis, as in 30% of patients, this value was missing.

Results

Patient characteristics

The EHS-PCI Registry enrolled a total of 46 064 PCI patients. The median age of the study cohort was 64 years and 74% were men. Fifty-one per cent of patients underwent PCI for (stabilized) acute coronary syndromes (ACS), and 49% had an elective procedure. In 94% of the patients, a stent was implanted; 46% of these stents were drug eluting. In 84% of the patients, percutaneous access was via the femoral and in 15% via the radial approach. Patients in the training and validation data sets had similar clinical and angiographic characteristics (*Table 1*). Patients were discharged after 2 days (inter-quartile range 1–4), 85.7% went home, 12.8% was transferred to another hospital, and 1.5% to a rehabilitation centre.

Determinants of in-hospital mortality in the training data set

In the training cohort, a total of 339 patients (1.5%) died during hospitalization. In univariable analysis, advanced age, particularly age above 80 years [OR 6.8; 95% confidence interval (CI) 4.2–11], haemodynamic instability (i.e. cardiac shock at admission or resuscitation prior to PCI) (OR 52; 95% CI 41–66), left ventricular function (LVF) ≤30% (OR 28; 95% CI 19–40), and STEMI (OR 24; 95% CI 16–35) were strongly associated with increased mortality risk (*Table 2*). The presence of three-vessel disease (OR 3.5; 95% CI 2.7–4.6) and the presence of left main disease (OR 4.2; 95% CI 3.1–5.7) were the most relevant angiographic characteristics for in-hospital death.

Mortality risk score

A total of 16 variables remained in the multivariable model for the prediction of in-hospital death (*Table 2*), among which haemodynamic instability at admission, STEMI, and age ≥80 years were most dominant. Ten variables were patient-related and could be obtained prior to the PCI procedure. Six factors were derived during angiography. The multivariable model translated in the scoring system is presented in *Figure 1*. There is a direct relation between the number of risk points and the estimated and observed mortality. For example, a 72-year-old (3 points) woman (2 points) with a prior stroke (2 points) but no known heart disease [thus no prior coronary artery bypass grafting (CABG), 4 points] who presents with STEMI (8 points) and left main disease (3 points) has a total risk score of 22 points. The observed in-hospital mortality risk among the patients with 22 risk points was 5.3% (20 of 376 patients), and the predicted risk (based on the model) was 3.8%.

As demonstrated in *Figures 2* and *3*, the majority of patients (≈90%) have a low mortality risk, i.e. a score of ≤20 corresponding with a mortality of <2%. A score of 21–26 (2–8.4% mortality) is present in ~7.5% of the patients and the remaining 2.5% of the patients is a high-risk population with in-hospital mortality over 7.5%, i.e. a score of ≥27.

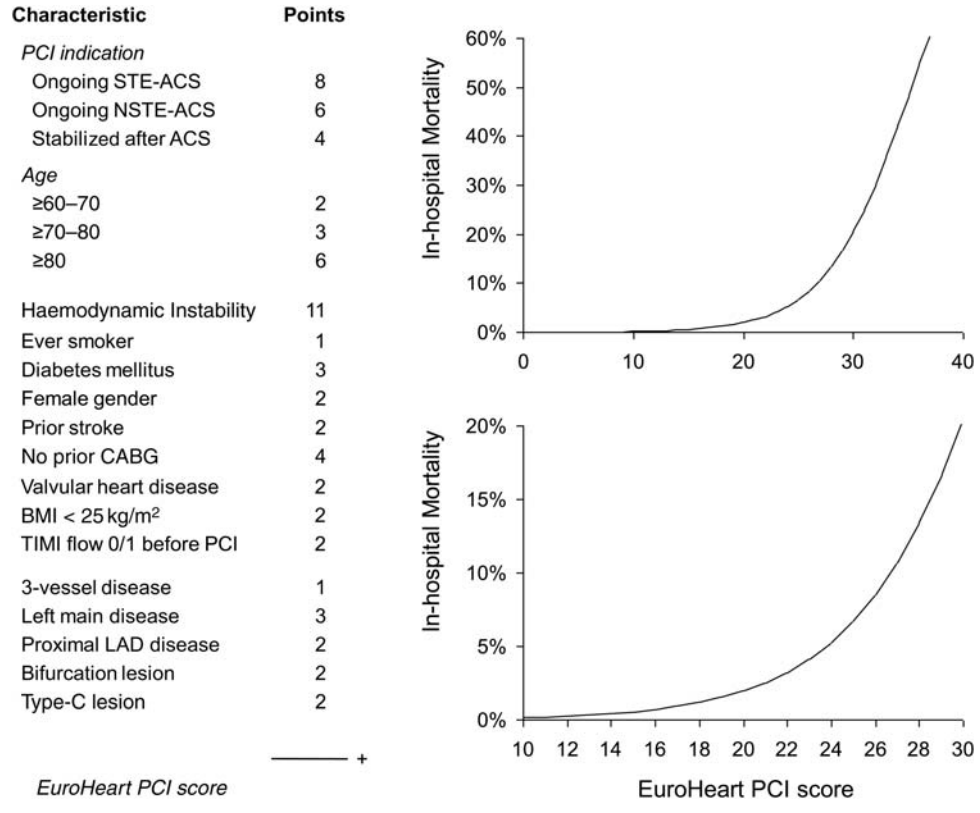

Figure 1 EuroHeart PCI score. Assigned integer scores.

Model performance

The multivariate training model has an excellent performance in terms of discrimination (*C*-index 0.91) and calibration (H–L *P*-value 0.93). When subsequently the risk score is created and applied to the training set, the *C*-index is 0.91 and H–L *P*-value 0.39. In the validation set, similar discrimination (*C*-index 0.90) and adequate calibration (H–L *P*-value 0.18) were observed (*Figure 4*).

We also investigated the model performance in different subgroups (*Table 3*) and compared the performance of the current model with others (*Table 4*).

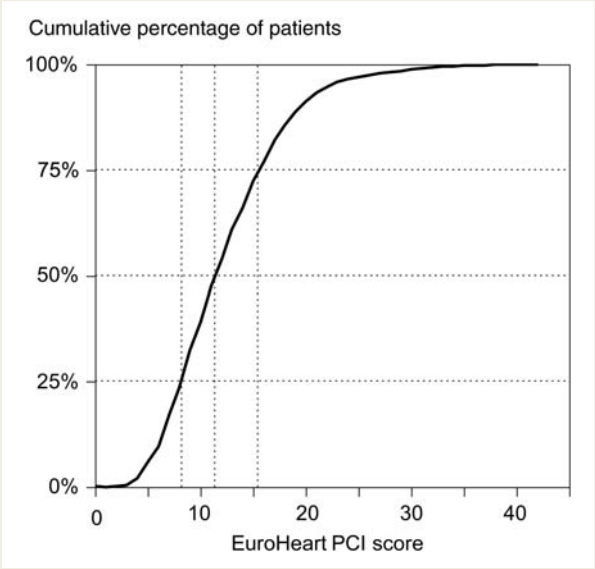

Figure 2 Distribution of assigned scores over the validation cohort.

Patients presenting with ST-elevation myocardial infarction

We performed a separate analysis of the 8060 patients who presented with ST elevation ACS to have a valid model for this high-risk population, since only a small proportion of the original data consist of high-risk patients.

From the original training and validation cohorts, the STEMI patients were selected, i.e. 4091 and 3969, respectively. In the training cohort, a total of 220 out of 4091 patients (5.4%) and in the validation cohort 203 out of 3969 (5.1%) died during hospitalization.

With multivariate analysis, 19 variables remained of significant influence. Particularly, haemodynamic instability at admission (OR 14; 95% CI 10–20), age ≥80 (OR 4.6; 95% CI 2.7–7.9), and left main disease (OR 2.1; 95% CI 1.2–3.7) were associated with a high in-hospital mortality risk (*Table 5*).

In this subpopulation, the area under the receiver-operating characteristic (ROC) curve was 0.86 with an H–L *P*-value of

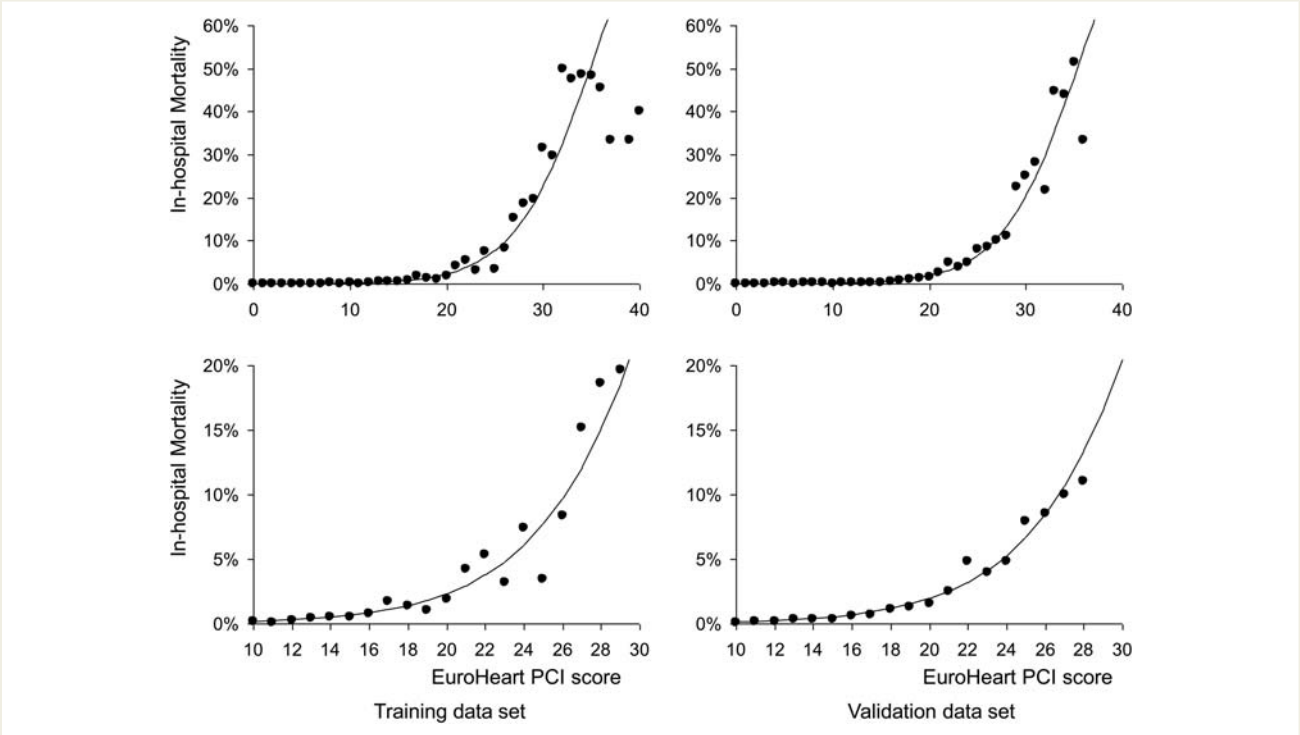

Figure 3 The EuroHeart PCI score model and observed in-hospital mortality. (Top left) Score in the training cohort. (Top right) Score in the validation cohort. (Bottom) Enlargement of patients with an intermediate score (10–30 points) in the training (left) and validation cohort (right) to better illustrate the transition point from low to intermediate risk. Score >40 is not illustrated as these score groups contain few (≤6) patients, which makes accurate prediction more difficult. Data points correspond to the observed mortality (*y*-axis) for patients with a particular score (*x*-axis), and line represents predicted mortality.

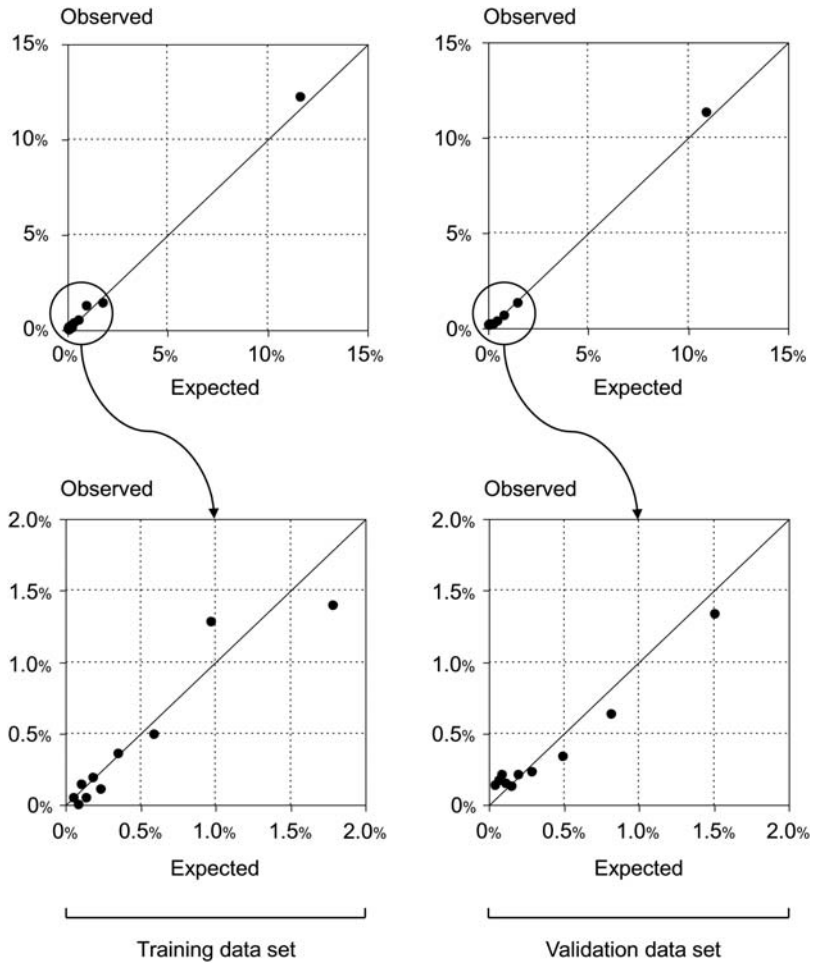

Figure 4 Expected vs. observed in-hospital mortality. (Top left) Training cohort. (Top right) Validation cohort. (Bottom) Enlargement of both cohorts. Rates were calculated with the Hosmer–Lemeshow goodness-of-fit test.

0.42, indicating a good discriminatory value in this high-risk subpopulation. Subsequently, we again created a simplified scoring model which was then tested in the training and validation data sets, the score ranged from 2 to 37 points (*Figure 5*).

In the training STEMI data, this simplified model demonstrated an area under the ROC curve of 0.86 with an H–L *P*-value of 0.75. In the STEMI validation data, similar discrimination (*C*-index 0.89) and calibration (H–L *P*-value 0.70) were observed. This acknowledges the validity of the separate STEMI model.

Discussion

We developed a risk score for in-hospital mortality after PCI based on clinical and angiographic data from the EHS-PCI database, with a high discriminatory value, and demonstrated its value in contemporary practice. Strong points of our model are the large sample size, pan-European multicentre approach, and the use of recent data from everyday clinical practice.

Previous work in patients undergoing CABG resulted in the EUROSCORE, a tool designed to assess the peri-operative risk for heart surgery.[19] Recently, this model was also tested in PCI

Table 3 Subgroup validation in validation cohort

Validated subgroup	Sample/mortality (*n*)	*C*-index	H–L *P*-value
Male	17 112/180	0.90	0.008
Female	5920/125	0.90	0.94
Age ≥70 years	7433/191	0.88	0.36
Age <70 years	15 599/114	0.89	0.003
Diabetes	5772/119	0.90	0.80
No diabetes	17 084/192	0.91	0.67
Patient in shock	574/157	0.74	0.85
Patient not in shock	22 458/148	0.82	0.21
PCI in ACS patient	11 710/279	0.91	0.85
PCI in elective patient	11 291/25	0.57	0.81
STEMI	3969/203	0.89	0.57
No STEMI	19 063/102	0.81	0.37

Although the H–L *P*-value is significant in men and patients <70, the maximum difference in observed and expected mortality per tentile is only four deaths; this was observed in the high-risk group (tentile 9/10 for both subgroups). H–L, Hosmer–Lemeshow; STEMI, ST-elevation myocardial infarction.

Table 4 Different risk models for percutaneous coronary intervention outcomes

Author and year of publication	AUC (C-index)	Predicted endpoint	Multi centre	DES used?	Remarks
This study	0.91	In-hospital mortality	Yes	Yes	Based on European population, contemporary practice
Peterson *et al.*[10] (2010)	0.93	In-hospital mortality	Yes	Yes	Based on North American population, contemporary practice
Singh *et al.*[8] (2008)	0.78 0.75	In-hospital MACE In-hospital mortality	No	N/A	Expansion of MCRS model with CAD-specific index
Madan *et al.*[3] (2008)	0.70	MACE at 30 days	No	Yes	Adding morbidity may have lowered discriminatory ability
Negassa *et al.*[4] (2007)	0.82	In-hospital mortality	Yes	N/A	3 factors in risk model
Halkin *et al.*[2] (2005)	0.83 0.79	30-day mortality 1-year mortality	Yes	No	Patients in shock or with complex coronary anatomy were excluded
Addala *et al.*[9] (2004)	0.78	6-month mortality	Yes	No	STEMI patients from various PAMI trials
Qureshi *et al.*[5] (2003)	0.87	In-hospital mortality	No	No	LVF and lesion characteristics not included
Shaw *et al.*[7] (2002)	0.89	In-hospital mortality	Yes	No	No systematic data auditing across participating centres Large data set (>100 000 PCIs)
Moscucci *et al.*[6] (2001)	0.90	In-hospital mortality	Yes	No	Little high-risk procedures Designed as bedside tool with only clinical parameters
Rihal *et al.*[12] (2000)	0.86	Death after PCI[a]	No	No	45% of procedures only balloon angioplasty

AUC, area under the ROC curve; DES, drug-eluting stent; MACE, major adverse cardiac event; N/A, not available; MCRS, Mayo Clinic Risk Score; CAD-specific index was developed to determine prognostic influence of co-morbid conditions.
[a]No specific time frame specified.

Table 5 Association between baseline characteristics and in-hospital mortality in the ST elevation acute coronary syndrome training cohort

	In-hospital death[a] (%)	Crude odds ratio and 95% CI	Multivariable adjusted odds ratio 95% CI
Age (years)	71/62	1.04 (1.03–1.06)	—
Age categorized (years)			
<50	2.4	1	—
≥50–60	3.1	1.3 (0.72–2.3)	—
≥60–70	5.4	2.3 (1.3–3.9)	1.9 (1.2–3.0)
≥70–80	7.9	3.4 (2.0–5.8)	2.8 (1.8–4.3)
≥80	11.9	5.4 (3.1–9.6)	4.6 (2.7–7.9)
Female	7.6/4.6	1.7 (1.3–2.3)	1.5 (1.06–2.2)
Body mass index	27/26	0.97 (0.94–1.01)	—
Body mass index <25	7.4/4.2	1.8 (1.3–2.4)	1.8 (1.3–2.5)
Hypertension	5.4/3.9	1.4 (1.04–1.9)	—
Hypercholesterolaemia	4.2/4.8	0.89 (0.67–1.2)	—
Diabetes mellitus	7.9/4.1	1.9 (1.4–2.6)	1.7 (1.2–2.4)
Ever smoker	4.3/4.6	0.88 (0.66–1.2)	1.8 (1.2–2.7)
Prior PCI	4.8/4.9	0.98 (0.62–1.6)	—
Prior CABG	4.9/5.2	1.06 (0.40–2.8)	0.30 (0.10–0.94)
Prior myocardial infarction	7.7/4.4	1.8 (1.3–2.4)	—

Continued

Table 5 *Continued*

	In-hospital death[a] (%)	Crude odds ratio and 95% CI	Multivariable adjusted odds ratio 95% CI
Congestive heart failure	8.8/4.7	1.9 (1.1–3.1)	—
Peripheral vascular disease	12.7/4.6	2.8 (1.7–4.6)	—
Prior stroke	11.3/4.7	2.5 (1.5–4.2)	1.6 (0.85–3.0)
Chronic renal insufficiency	10.7/4.8	2.3 (1.1–4.5)	—
Valvular heart disease	12.5/4.8	2.7 (1.07–6.9)	—
Number of diseased vessels			
1	3.3	1	—
2	5.6	1.7 (1.2–2.5)	1.4 (0.92–2.0)
3	9.1	2.9 (2.1–4.1)	1.5 (1.01–2.3)
Left main	20.4/4.8	5.1 (3.4–7.7)	2.1 (1.2–3.7)
Proximal LAD diseased	8.0/3.9	2.1 (1.6–2.8)	1.4 (1.01–2.0)
LAD is target vessel	6.3/4.7	1.4 (1.04–1.8)	1.4 (0.96–1.9)
Bifurcation lesion	8.7/5.3	1.7 (1.2–2.5)	1.4 (0.93–2.2)
Type-C lesion	8.1/3.9	2.2 (1.6–2.9)	1.5 (1.08–2.0)
PCI indication			
Primary PCI (<24 hrs)	5.3	1	—
Rescue PCI	7.0	1.35 (0.83–2.2)	—
Facilitated PCI	4.1	0.75 (0.33–1.7)	—
TIMI flow 0/1 before PCI	6.3/3.5	1.9 (1.3–2.6)	1.5 (1.05–2.3)
Haemodynamic instability	30.4/2.7	17 (13–23)	14 (10–20)
Left ventricular function[b]			
Class I (>50%)	1.9	1	—
Class II (31–50%)	4.0	2.2 (1.3–3.6)	—
Class III (≤30%)	26.8	19 (11–32)	—
Ischaemic time (h)			
0–3	4.7	1	—
3–6	4.8	1.03 (0.71–1.5)	—
6–12	5.1	1.09 (0.71–1.7)	—
>12	6.4	1.4 (0.90–2.1)	1.4 (0.92–2.1)

Continuous data (age, BMI) are presented as median values; dichotomous data are presented as percentages. Qualitative estimated based on 4091 patients.
[a]For in-hospital mortality, data represent mortality when variable is present (first number) or absent (second number).
[b]LVF was not included in the multivariable analyses as 36% of patients had missing data.

and demonstrated a good discriminatory value.[20] However, the EUROSCORE includes various operation-related factors that per definition do not apply to PCI. Thus, for PCI patients, not all items that compose the score can be filled, which, again per definition, results in inappropriate risk estimation.

These limitations were overcome by the recent NCDR model.[10] To avoid unnecessary risk models, we tried to validate this model on our data; there are some limitations however. The focus in data collection in the EHS-PCI survey was different from the NCDR data. As a result, we did not have information on three (out of eight) variables, i.e. glomerular filtration rate, New York Heart Association class, and chronic lung disease. Furthermore, the NCDR classification of the indication for PCI was different. With these limitations, we found a *c*-statistic of 0.89 with an H–L *P*-value of 0.05. Thus, discrimination is good, but calibration is poor.

Our model overcomes these limitations and may therefore be a good first step to create a specific European risk score to assess the peri-procedural risk of PCI. Next, it might be used as a benchmark tool to compare different hospitals. However, additional testing in a separate clinical cohort with new data may be considered beforehand.

Subgroup analysis revealed that our model is less useful to predict mortality in patients who undergo an elective procedure, i.e. not ACS-related. Apparently, it is difficult to predict events in this group as the mortality risk is very low (25 events in 11 291 patients = 0.22%). Perhaps, we have to accept that mortality risk in elective procedures cannot be predicted with classical risk

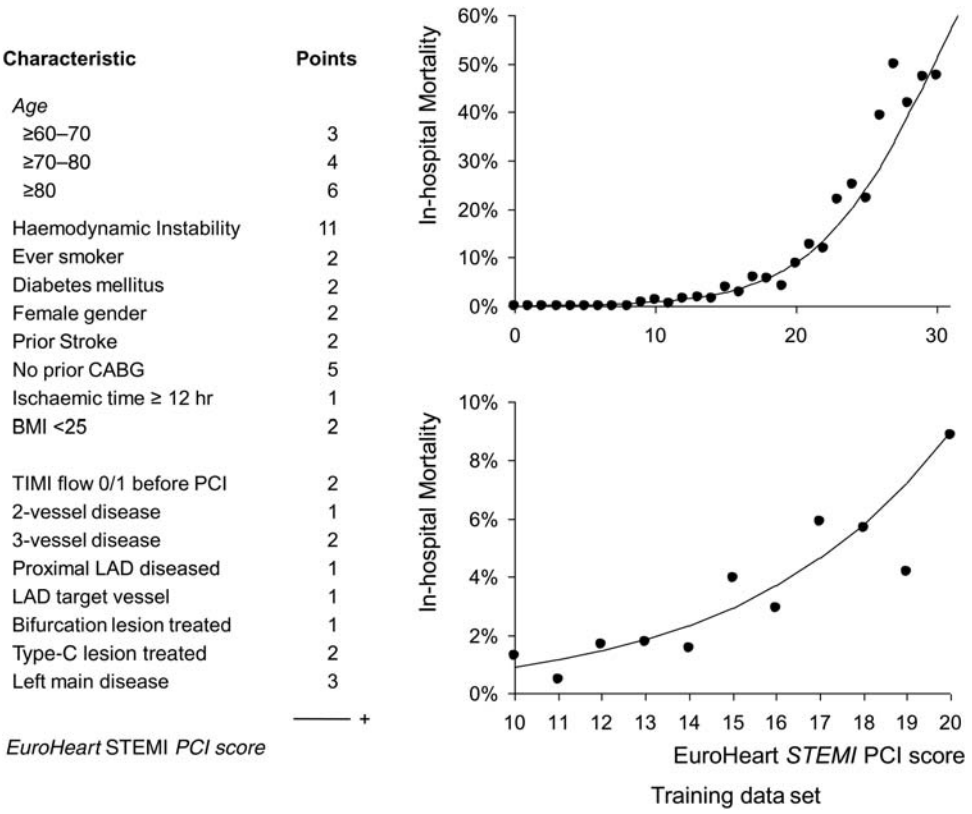

Figure 5 EuroHeart *STEMI* PCI score. Assigned integer scores. Score until 31 points; Scores 32–37 are left out as these contained only few patients (≤13).

factors, but might be more dependent on other factors such as operator experience or (contrast) allergies.

Another point of interest is that the tentile of patients with the highest risk has a mortality of ~10%. Perhaps that further stratification of this subcohort may improve the calibration.

Major determinants in our risk model are haemodynamic instability, STEMI, age ≥80, and three-vessel disease. Singh *et al.*[21] gave an overview of variables used in different risk scores. The main factors they described are also included in our model. However, additional factors from their analysis such as RF and peripheral artery disease did not contribute significantly in our multivariate analysis. Possibly, this is a consequence of the limitations of a survey in which these data might not have been collected as precisely as in a clinical trial. Indeed, non-collection of variables is a problem for any risk model, particularly when it is externally validated.

It appeared that prior CABG has a protective effect in our score model. Interestingly, out of 2857 patients with prior CABG, 2042 (72%) had the intervention only in their native vessels. Therefore, we might speculate that these interventions were done under the protection of patent bypass grafts, resulting in better outcomes.

The protocol did not mandate serial electrocardiograms or blood sampling for the determination of cardiac enzymes. As per design, it was the intention to minimize the impact of the protocol on routine procedures. Since we realize that registry designs are susceptible to observer bias, especially with regard to 'soft' parameters, we chose the incidence of all-cause mortality during hospitalization as the primary endpoint of this study. Particularly, this is the clinically most relevant endpoint for patients.

The predictive value of future risk models might be further enhanced when they are also fitted with serum markers such as admission glucose,[22] C-reactive protein,[23] and N-terminal-pro-brain natriuretic peptide.[24]

It is important to recognize that interventional cardiology is under continuous development and new techniques arise which will require adaptation of existing predictive models. However, it might be sufficient to re-validate a powerful existing model instead of developing a complete new one.

Limitations

Our analysis has several limitations that should be mentioned. Since our model predicts in-hospital mortality, this can be influenced with different discharge policies. For example, referral centres where patients quickly after PCI are transported to a nearby hospital for further recovery may have low mortality figures as patients spend only several hours in that particular referral centre (this was applicable to 12.8% of patients). The same might be relevant for centres without on-site surgical backup when emergency CABG as a result of the PCI is required.

However, only in 49 patients (0.1%), emergency CABG was performed.

Another matter is selection bias as to who receives angiography. It is conceivable that clinicians decide not to perform angiography as they consider that as a result of the advanced age, particularly over 80, PCI risk is already too high. Knowledge of the coronary anatomy would not change their therapy. Consequently, PCI risk in frail octogenarians may actually be underestimated.

Our model uses only patient-related factors; therefore, we are not informed on operator experience and procedure volumes, which also affect outcomes. In small hospitals, for example, experience may be lower due to small sample size. When these are taken into account, the predictive value (as expressed by the *C*-index) of future models might further increase. However, then the model is not suitable for benchmarking purposes. Additional parameters, such as heart rate or novel biomarkers, might give an even better discriminatory power, but were regrettably not available.

Conclusion

We have developed a risk score to predict in-hospital mortality in PCI patients. This model is based on a large patient sample, pan-European multicentre approach, and recent data from everyday clinical practice, which strengthens its applicability. As it uses clinical and angiographic data, it is easy to implement in clinical practice to estimate the in-hospital mortality risk after PCI.

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