Original Article

A risk score to predict in-hospital mortality in patients with acute coronary syndrome at early medical contact: results from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome (CCC-ACS) Project

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Background: A number of models have been built to evaluate risk in patients with acute coronary syndrome (ACS). However, accurate prediction of mortality at early medical contact is difficult. This study sought to develop and validate a risk score to predict in-hospital mortality among patients with ACS using variables available at early medical contact.

Methods: A total of 62,546 unselected ACS patients from 150 tertiary hospitals who were admitted between 2014 and 2017 and enrolled in the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome (CCC-ACS) project, were randomly assigned (at a ratio of 7:3) to a training dataset (n=43,774) and a validation dataset (n=18,772). Based on the identified predictors which were available prior to any blood test, a new point-based risk score for in-hospital death, CCC-ACS score, was derived and validated. The CCC-ACS score was then compared with Global Registry of Acute Coronary Events (GRACE) risk score.

Results: The in-hospital mortality rate was 1.9% in both the training and validation datasets. The CCC-ACS score, a new point-based risk score, was developed to predict in-hospital mortality using 7 variables that were available before any blood test including age, systolic blood pressure, cardiac arrest, insulin-treated diabetes mellitus, history of heart failure, severe clinical conditions (acute heart failure or cardiogenic shock), and electrocardiographic ST-segment deviation. This new risk score had an area under the curve (AUC) of 0.84 (P=0.10 for Hosmer-Lemeshow goodness-of-fit test) in the training dataset and 0.85 (P=0.13 for Hosmer-Lemeshow goodness-of-fit test) in the validation dataset. The CCC-ACS score was comparable to the Global Registry of Acute Coronary Events (GRACE) score in the prediction of in-hospital death in the validation dataset.

Conclusions: The newly developed CCC-ACS score, which utilizes factors that are acquirable at early medical contact, may be able to stratify the risk of in-hospital death in patients with ACS.

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Keywords: Acute coronary syndrome (ACS); in-hospital death; risk score; early medical contact

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Introduction

Ischemic heart disease (IHD) is the leading cause of death globally (1,2). In 2018, the annual mortality ratio among Chinese patients with IHD exceeded 110/100,000, and it is steadily increasing (3). Acute coronary syndrome (ACS) is a severe manifestation of IHD with a prognosis that varies significantly among patients. Therefore, risk stratification is critical for decision-making and management implementation, such as timely invasive strategies for patients at high risk.

Several risk scores for ST-segment elevation myocardial infarction (STEMI), non–ST-segment elevation ACS (NSTE-ACS), and unselected ACS have been developed (4-8), among which some have been recommended by clinical guidelines (9-12). However, the existing risk score systems have some limitations (13). Firstly, most of them were developed prior to or during the early phase of the drug-eluting stent era, and minority of patients underwent percutaneous intervention, thus the discrimination power was relatively poor in those patients. Secondly, acquiring the variables for these risk scores is time consuming, which limits their utility at the point of early medical contact. Further, some risk scores at early medical contact were available, however some ACS patients at high risk were excluded in the registries developing risk score.

The present study aimed to develop and validate a simple and accurate risk score to predict in-hospital death in unselected patients with ACS at early medical contact by using data from the CCC-ACS registry, which represents the real-world practice in the drug-eluting stent era. We present the following article in accordance with the TRIPOD reporting checklist (available at http://dx.doi.org/10.21037/atm-21-31).

Methods

Study protocol

The CCC-ACS project design has been reported previously (14). Briefly, the American Heart Association (AHA) and Chinese Society of Cardiology (CSC) launched the CCC-ACS project in 2014 as a nationwide hospital-based quality improvement registry program to improve the quality of care of patients with ACS. The present study was approval by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University. As the study used data from a retrospective registry, the requirement for informed consent was waived. All patient information was anonymized and de-identified before analysis. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013).

Study population and data collection

From November 1, 2014 to June 30, 2017, CCC-ACS phases I and II enrolled 63,641 patients with ACS from 150 tertiary hospitals, which represented the highest level of medical care in the 7 geographical regions of China (Northern, Northeast, Eastern, Central, Southern, Southwest, and Northwest China).

Data were collected by trained data abstractors (medical doctors, nurses, medical postgraduates, and clinical research coordinators) at the participating hospitals through a web-based data collection platform (Oracle Clinical Remote Data Capture, Oracle). At each hospital, the first 20–30 ACS patients each month were consecutively enrolled. To ensure that consecutive cases were enrolled, quality audits were performed by third-party clinical research associates. The accuracy and completeness of the clinical data were verified using documents from approximately 5% of enrolled cases, who were randomly selected.

Definitions

Briefly, STEMI and non–ST-segment elevation myocardial infarction (NSTEMI) were defined according to the 2010 CSC STEMI guidelines (15) and the 2012 CSC NSTE-ACS guidelines (16), respectively. Unstable angina (UA) was defined as reported previously (14). Acute heart failure (AHF) and cardiogenic shock (CS) were defined according

to the Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2014 (17), based on the patient's clinical condition recorded in the medical documentation on hospital admission. The endpoint was in-hospital death. Troponin I (TnI), troponin T (TnT), and creatine kinase MB isoenzyme (CK-MB) elevation was considered when the levels of these markers exceeded the upper level of normal (ULN) of the corresponding local laboratory. Estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease equation.

Statistical analysis

Statistical analyses were performed in SAS (version 9.4, SAS Institute, Cary, North Carolina). Data were presented as the mean ± standard deviation (SD) for normally distributed data, or medians and interquartile ranges (IQR) for non-normally distributed data. Normally and non-normally distributed variables were compared using Student's t-test and the Mann-Whitney U test, respectively. Categorical data were expressed as numbers (%). Pearson's χ^2 test or Fisher's exact test were used for categorical data, as appropriate. Using Proc Surveyselect (SAS, SAS Institute, Cary, North Carolina), the simple random sampling method was employed to randomly assign patients to a training dataset or a validation dataset at a ratio of 7:3. The CCC-ACS risk score was constructed by fitting demographic, medical history, clinical, and electrocardiographic variables, which were selected based their clinical significance and the findings of previous studies, as well as on their availability during early medical contact. Variables obtained by laboratory tests were not considered for entry into the model. Potential risk factors were screened through univariate logistic regression analysis with the level of significance set at P<0.05. Independent predictors were identified by performing multivariate logistic regression analysis. Only variables with a P value of <0.05 in the multivariate analysis were entered into the final model. The integer score was generated by multiplying the β coefficient of each selected variable by a constant and rounding the product to the nearest integer. Discrimination and calibration were assessed using the area under the receiver operating characteristic (ROC) curve (AUC) and the Hosmer-Lemeshow (H-L) goodness-of-fit test, respectively. Differences in the discriminatory power between the CCC-ACS score and the Global Registry of Acute Coronary Events (GRACE) score were evaluated using the χ^2 test. All P values were 2-tailed, and a P value of <0.05 was considered to represent statistical significance.

Results

There were 63,641 unselected ACS patients analyzed in this study, 44,549 patients initially assigned to the training dataset and 19,092 to the validation dataset. During the modeling process, 775 (1.7%) and 320 (1.7%) patients were excluded from the training and validation cohorts, respectively, due to having missing values for the finally incorporated variables (age, systolic blood pressure, cardiac arrest, and severe clinical conditions). The remaining 43,774 and 18,772 patients were enrolled in the final analyses (*Figure 1*).

In total, 1,181 in-hospital deaths occurred among the study patients, including 824 (1.9%) in the training dataset and 357 (1.9%) in the validation dataset. As shown in *Table 1*, except for prior dialysis (0.2% *vs*. 0.4%, P=0.002), there were no significant differences in demographic, clinical, laboratory, electrocardiographic, or therapeutic characteristics, or in-hospital outcomes between the training and validation cohorts.

In the training dataset, the in-hospital death group had higher proportions of patients with STEMI, a history of heart failure, hypertension, diabetes mellitus, insulin-treated diabetes mellitus (ITDM), previous dialysis, ST-segment deviation, elevated CK-MB, and 5-fold elevated TNT or TNI. Furthermore, these patients were less likely to smoke or have a history of percutaneous coronary intervention (PCI). Patients in the in-hospital death group in the training dataset were also older, had higher heart rates and serum creatinine levels, and lower systolic blood pressure (SBP), diastolic blood pressure (DBP), and eGFR. Moreover, patients who died in hospital were more likely to present with cardiac arrest, AHF, and CS at admission (*Table 2*).

Development and Validation of the CCC-ACS score

The results of univariate and multivariate logistic regression analyses are displayed in Table S1. After univariable and multivariable selection, 7 variables emerged as predictors of mortality, including age, SBP, cardiac arrest, ITDM, history of heart failure, severe clinical conditions at admission (AHF and/or CS), and ST-segment deviation. The scores assigned to each variable based on their estimated β coefficients in the training dataset are shown in *Table 3*. The AUC for the original model was 0.84, and the χ^2 statistic for calibration was 11.48 (P=0.18).

The scores for each predictor based on their estimated β coefficients are presented in *Figure 2*. The sum of the score which could theoretically range from 0 to 36, could be used to estimate the risk of in-hospital death for individual patients. In

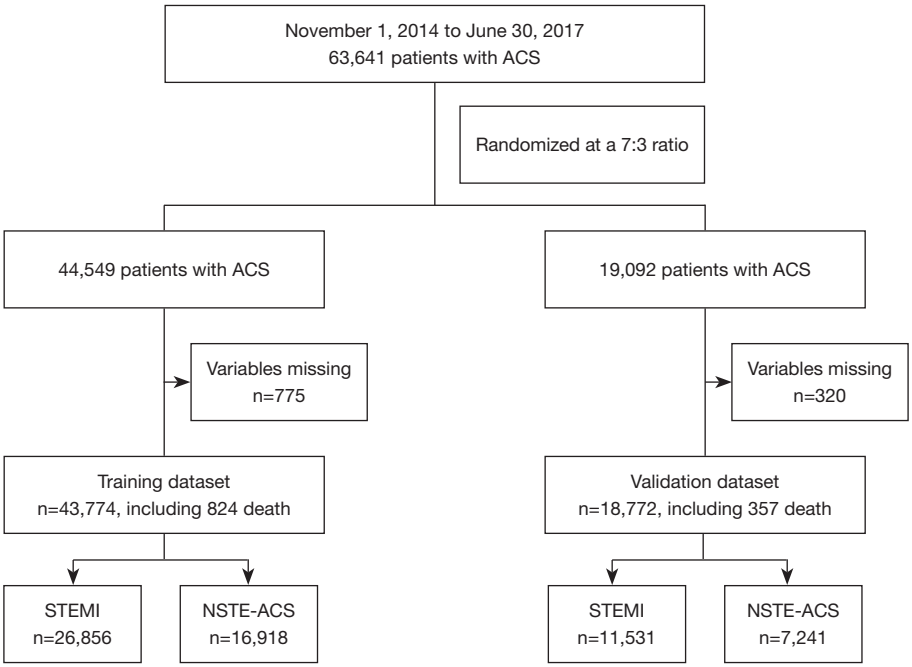

Figure 1 Study flow chart. The enrolled study population was divided into a training dataset and a validation dataset. ACS, acute coronary syndrome. STEMI, ST-segment elevation myocardial infarction. NSTE-ACS, non–ST-segment elevation acute coronary syndromes.

Table 1 Patient clinical characteristics

Characteristics	Total (n=62,546)	Training (n=43,774)	Validation (n=18,772)	P value
Age, years	63±12	63±13	63±12	0.598
Female, n (%)	15,678 (25.1)	10,967 (25.1)	4,711 (25.1)	0.911
Type of ACS, n (%)				0.860
STEMI	38,387 (61.4)	26,856 (61.4)	11,531 (61.4)	
NSTE-ACS	24,159 (38.6)	16,918 (38.6)	7,241 (38.6)	
Medical history, n (%)				
Smoking	27,052 (43.3)	18,912 (43.2)	8,140 (43.4)	0.713
History of MI	4,823 (7.7)	3,385 (7.7)	1,478 (7.7)	0.755
History of CABG	316 (0.5)	210 (0.5)	106 (0.6)	0.170
History of PCI	4,777 (7.6)	3,378 (7.7)	1,399 (7.5)	0.254
History of heart failure	1,246 (2.0)	8,47 (1.9)	399 (2.1)	0.118
Hypertension	33,094 (52.9)	23,170 (52.9)	9,924 (52.9)	0.858
Diabetes mellitus	13,859 (22.2)	9,716 (22.2)	4,143 (22.1)	0.729
ITDM	3,655 (5.8)	2,562 (5.9)	1,093 (5.8)	0.882
Prior dialysis	181 (0.3)	108 (0.2)	73 (0.4)	0.002
Clinical conditions at admission				
GRACE score*	144±37	144±37	144±37	0.719

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Total (n=62,546)	Training (n=43,774)	Validation (n=18,772)	P value
Cardiogenic shock, n (%)	1,893 (3.0)	1,357 (3.1)	536 (2.9)	0.102
AHF without cardiogenic shock, n (%)	5,584 (8.9)	3,861 (8.8)	1,723 (9.2)	0.150
Cardiac arrest, n (%)	1,198 (1.9)	817 (1.9)	381 (2.0)	0.172
HR*, beats/min	77±16	77±16	77±16	0.816
SBP, mmHg	130±23	130±24	130±23	0.259
DBP, mmHg	78±14	78±14	78±14	0.504
Killip class*, n (%)				0.377
I	41,007 (70.2)	28,649 (70.0)	12,358 (70.4)	
II–III	15,058 (25.8)	10,601 (25.9)	4,457 (25.4)	
IV	2,377 (4.1)	1,649 (4.0)	728 (4.1)	
ST-segment deviation, n (%)	42,795 (68.4)	29,964 (68.5)	12,831 (68.4)	0.647
Laboratory variables				
Scr† μmol/L	76 (64, 93)	76 (64, 93)	76 (64, 93)	0.168
eGFR†, mL/min/1.73 m^2	90.89±30.18	91.00±31.85	90.63±31.68	0.181
Elevated TnT or TnI‡, n (%)	46,944 (84.1)	32,792 (84.0)	14,152 (84.4)	0.280
5×elevated TnT or TnI‡, n (%)	40,540 (72.6)	28,298 (72.5)	12,242 (73.0)	0.233
Elevated CK-MB‡, n (%)	37,026 (65.3)	25,892 (65.2)	11,134 (65.5)	0.596
LVEF§ %	55.13±10.24	55.19±10.20	55.01±10.34	0.077
In-hospital treatment, n (%)				
Aspirin	59,201 (94.7)	41,393 (94.6)	17,808 (94.9)	0.121
P2Y12 antagonist	59,620 (95.3)	41,720 (95.3)	17,900 (95.4)	0.798
Statins	58,642 (93.8)	41,042 (93.8)	17,600 (93.8)	0.992
ACEIs or ARBs	29,863 (47.7)	20,899 (47.7)	8,964 (47.8)	0.983
β-blocker	34,587 (55.3)	24,254 (55.4)	10,333 (55.0)	0.403
PCI	45,198 (72.3)	31,697 (72.4)	13,501 (71.9)	0.210
CABG	661 (1.1)	479 (1.1)	182 (1.0)	0.162
In-hospital adverse outcomes, n (%)				
Death	1,181 (1.9)	824 (1.9)	357 (1.9)	0.870

*, GRACE score and Killip class were not available for 11.8% (7,351/62,546) and 6.6% (4,104/62,546) of patients with ACS in the study population, respectively. HR was not available for 19 patients with ACS in the study population; †, 2.9% (1,836/62,546) of patients did not have Scr and 2.9% (1,836/62,546) of patients did not have eGFR in the study population; ‡, TnT or TnI were not available for 10.8% (6,739/62,546) of patients with ACS, and elevated CK-MB were not available for 9.4% (5,856/62,546) of patients with ACS in the study population, respectively; §, LVEF was not available for 22.8% (14,255/62,546) of patients with ACS in the study population. ACEI, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; AHF, acute heart failure; ARBs, angiotensin receptor blockers; CABG, coronary artery bypass grafting; CK-MB, creatine kinase-MB; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GRACE score, Global Registry of Acute Coronary Events risk score; HR, heart rate; ITDM, insulin-treated diabetes mellitus; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTE-ACS, non–ST-segment elevation acute coronary syndromes; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; Scr, serum creatinine; STEMI, ST-segment elevation myocardial infarction.

Table 2 Patient clinical characteristics in the training dataset

Characteristics	Survived (n=42,950)	Died (n=824)	P value
Age, years	63±12	72±11	<0.001
Female, n (%)	10,664 (24.8)	303 (36.8)	<0.001
Type of ACS, n (%)			<0.001
NSTE-ACS	16,684 (38.8)	234 (28.4)	
STEMI	26,266 (61.2)	590 (71.6)	
Medical history, n (%)			
Smoking	18,684 (43.5)	228 (27.7)	<0.001
History of MI	3,313 (7.7)	72 (8.7)	0.276
History of CABG	204 (0.5)	6 (0.7)	0.297
History of PCI	3,332 (7.8)	42 (6.0)	0.020
History of heart failure	788 (1.8)	59 (7.2)	<0.001
Hypertension	2,267 (52.8)	483 (58.6)	<0.001
Diabetes mellitus	9,458 (22.0)	258 (31.3)	<0.001
ITDM	2,470 (5.8)	92 (11.2)	<0.001
Prior dialysis	100 (0.2)	8 (1.0)	<0.001
Clinical conditions at admission			
GRACE score*	143±36	194±41	<0.001
Cardiogenic shock, n (%)	1,107 (2.6)	250 (30.3)	<0.001
AHF without cardiogenic shock, n (%)	3,532 (8.2)	329 (40.0)	<0.001
Cardiac arrest, n (%)	636 (1.5)	181 (22.0)	<0.001
HR*, beats/min	77±16	89±23	<0.001
SBP, mmHg	130±23	118±30	<0.001
DBP, mmHg	78±14	71±17	<0.001
Killip class*, n (%)			<0.001
I	28,362 (70.7)	287 (37.0)	
II–III	10,342 (25.8)	259 (33.4)	
IV	1,419 (3.5)	230 (29.6)	
ST-segment deviation, n (%)	29,278 (68.2)	686 (83.3)	<0.001
Laboratory variables			
Scr†, μmol/L	76 (64, 92)	100 (76, 143)	<0.001
eGFR†, mL/min/1.73m^2	91.47±31.61	65.08±34.25	<0.001
Elevated TnT or TnI‡, n (%)	32,114 (83.8)	678 (96.4)	<0.001
5× Elevated TnT or TnI‡, n (%)	27,676 (72.2)	622 (88.5)	<0.001
Elevated CK-MB‡, n (%)	25,274 (64.9)	618 (85.2)	<0.001
LVEF§ %	55±10	44±12	<0.001

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	Survived (n=42,950)	Died (n=824)	P value
In-hospital therapy, n (%)			
Aspirin	40,701 (94.8)	692 (84.0)	<0.001
P2Y12 antagonist	41,007 (95.5)	713 (86.5)	<0.001
Statins	40,407 (94.1)	635 (77.1)	<0.001
ACEIs or ARBs	20,671 (48.1)	228 (27.7)	<0.001
β-blocker	23,977 (55.8)	277 (33.6)	<0.001
PCI	31,384 (73.1)	313(38.0)	<0.001
CABG	406 (0.9)	73 (8.9)	<0.001

*, GRACE score and Killip class were not available for 11.7% (5,123/43,774) and 6.6% (2,875/43,774) of patients with ACS in the training dataset, respectively. HR was not available for 15 patients with ACS in the training dataset; †, 2.9% (1,257/43,774) of patients did not have Scr and 2.9% (1,257/43,774) of patients did not have eGFR in the training dataset; ‡, TnT or TnI were not available for 10.8% (4,740/43,774) of patients with ACS, and elevated CK-MB were not available 9.3% (4,089/43,774) of patients with ACS in the training dataset; §, LVEF was not available for 23.1% (10,102/43,774) of patients with ACS in the training dataset. ACEI, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; AHF, acute heart failure; ARBs, angiotensin receptor blockers; CABG, coronary artery bypass grafting; CK-MB, creatine kinase-MB; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GRACE score, Global Registry of Acute Coronary Events risk score; HR, heart rate; ITDM, insulin-treated diabetes mellitus; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTE-ACS, non-ST-segment elevation acute coronary syndromes; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; Scr, serum creatinine; STEMI, ST-segment elevation myocardial infarction.

the training dataset, the actual obtained scores ranged from 0 to 31. The CCC-ACS score displayed good discrimination ability (AUC: 0.84) and calibration (χ^2=13.43, P=0.10) (*Figure 3A*). In the validation dataset, the actual obtained scores ranged from 0 to 29, and the CCC-ACS score also displayed good discrimination ability (AUC: 0.85) and calibration (χ^2=12.63, P=0.13, Brier score =0.02) (*Figure 3B*).

Based on the obtained risk scores for in-hospital death, the training dataset was further categorized into the following 3 groups: low risk (score ≤12, n=40,452), moderate risk (score: 13–20, n=2,919), and high risk (score≥21, n=403). The event rate was 0.96%,10.11%, and 34.49%, respectively (*Figure 4*). The validation dataset was also categorized into 3 groups: low risk (score ≤12, n=17,323), moderate risk (score: 13–20, n=1,269), and high risk (score ≥21, n=180). The event rate was 0.96%,10.01%, and 35.56%, respectively (*Figure 4*).

Performance in subgroups

The CCC-ACS score also exhibited good discrimination ability after the patients were divided into subgroups according to sex, ACS type, and previous PCI or not (Table S2). After the exclusion of 2,228 patients who had missing values for GRACE variables, the remaining 16,544 patients in the validation dataset were used to compare the performances of the CCC-ACS score and the GRACE score. The 2 scores performed comparably in the prediction of in-hospital death (AUC: CCC-ACS 0.84, 95% CI: 0.81–0.86 *vs.* GRACE 0.83, 95% CI: 0.81–0.86, P=0.69). The χ^2 statistics for the CCC-ACS and GRACE scores were 5.12 (P=0.74) and 8.44 (P=0.39) respectively, showing the good calibration for in-hospital mortality.

Discussion

In the present study, a new in-hospital mortality risk score (CCC-ACS score) was developed and validated. The CCC-ACS risk score comprises 7 variables [age, cardiac arrest, ITDM, history of heart failure, severe clinical conditions at admission (AHF and/or CS), SBP, and ST-segment deviation], and demonstrated good discrimination ability and calibration in predicting the risk of in-hospital death for unselected ACS patients at early medical contact.

Several risk scores have been developed for risk stratification in patients with ACS. Among them, the Thrombolysis in Myocardial Infarction (TIMI) and GRACE scores are recommended by clinical guidelines and are widely applied in clinical practice. Both of these risk scoring systems can provide important information for predicting prognosis and determining the timing of interventions;

Table 3 CCC-ACS risk sore final model

Predictors	β coefficient	χ^2	OR	95% CI	P value
Cardiac arrest	1.8500	244.94	6.36	5.05–8.02	<0.0001
History of heart failure	0.4766	9.04	1.61	1.18–2.20	0.0026
ITDM	0.6845	31.79	1.98	1.56–2.52	<0.0001
ST-segment deviation	0.6148	39.37	1.85	1.53–2.24	<0.0001
Clinical conditions at admission					
No AHF or CS (reference)	–	–	–	–	–
AHF without CS	1.0462	103.74	2.85	2.33–3.48	<0.0001
CS	1.9255	275.19	6.86	5.46–8.61	<0.0001
SBP					
≥140 (reference)	–	–	–	–	–
100–139	0.3216	12.18	1.38	1.15–1.65	0.0005
80–99	0.7974	39.53	2.22	1.73–2.85	<0.0001
<80	1.1011	30.27	3.01	2.03–4.45	<0.0001
Age (years)					
<60 (reference)	–	–	–	–	–
60–69	0.6075	23.69	1.84	1.44–2.35	<0.0001
70–79	1.3572	134.96	3.89	3.09–4.89	<0.0001
80–89	1.8523	216.36	6.37	4.98–8.16	<0.0001
≥90	2.5142	108.12	12.36	7.69–19.85	<0.0001

AHF, acute heart failure; CCC-ACS Risk Score: Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Risk Score; CS, cardiogenic shock; ITDM, insulin-treated diabetes mellitus; SBP, systolic blood pressure.

however, they have some limitations (13). The TIMI risk score was derived from clinical trials and thus has inherent bias due to the exclusion of high-risk patients. The GRACE score was developed from a large-scale unbiased multi-center registry and was validated in external datasets; thus, it has an excellent performance when applied to the general population. Nevertheless, it has been found to lack accuracy for patients undergoing PCI (6), which may because less than 30% of patients in the GRACE (18) and Global Use of Strategies to Open Occluded Coronary Arteries IIB (GUSTO IIB) studies underwent PCI (19,20). Furthermore, in the contemporary era, PCI has been used more widely, and its use has been accompanied by advances in medical treatments, such as P2Y12 antagonist, statin, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), and β-blockers. In the real-world registry used in the present study, which was compiled in the drug-eluting stent era, 72.3% of ACS patients underwent PCI. Therefore, an updated risk score that is fitting of current clinical practice is needed to supplement the use of previous scoring systems.

The CCC-ACS risk score shares 5 variables (age, cardiac arrest, SBP, severe clinical conditions at admission, and ST-segment deviation) with previous risk scores (4,21), and includes 2 (ITDM and history of heart failure) newly introduced variables. ITDM has been proven as a risk factor for adverse clinical outcomes in patients with NSTE-ACS or those undergoing PCI (22,23). Patients with ITDM may have suffered a longer course of diabetes mellitus and may therefore represent a more severe disease condition (24). History of heart failure, another newly incorporated variable, has also been proved to be associated with in-hospital, 6-month, and 1-year mortality in ACS patients (25-28). A majority of previous studies have focused on AHF in patients with ACS, but a history of heart failure is also important and of independent value. ACS

1. Find the score for each predictor

Age, yrS	Points	SBP, mmHg	Points	Severe condition at admission	Points
<60	0	≥140	0	No AHF or CS	0
60~70	2	100~140	1	AHF without CS	4
70~80	5	80~100	3	CS	8
80~90	7	<80	4		
≥90	10				

Other Risk Factors	Points
Cardiac arrest	7
History of heart failure	2
Insulin treated diabetic mellitus	3
ST-segment deviation	2

2. Sum the score for all predictors

3. Look up risk corresponding to total score

Total Points	≤4	8	12	16	20	24	>24
Probability of in-hospital mortality	0.30%	1.25%	3.51%	10.23%	20.55%	34.51%	50.88%

Figure 2 Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome risk score (CCC-ACS score). SBP, systolic blood pressure. AHF, acute heart failure. CS, cardiogenic shock.

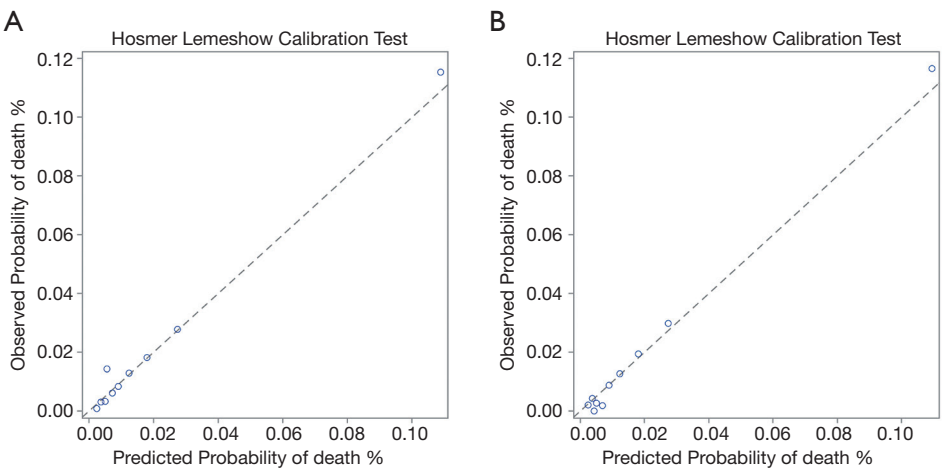

Figure 3 Calibration of Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome risk score (CCC-ACS score). (A) Calibration of CCC-ACS score in the training dataset. (B) Calibration of CCC-ACS score in the validation dataset. The diagonal line indicates perfect calibration.

patients with a history of heart failure may have lower cardiac reserve at baseline, and receive evidence-based therapies, such as β-blockers, ACEIs, and PCI, less frequently (25). Although some studies have associated a history of myocardial infarction with adverse outcomes (29,30), it was not found to be an independent predictor after regression in the current analysis. This may be because, at least in part, a history of heart failure is correlated with and more powerful predictor than a history of myocardial infarction. Cardiac markers (TnI, TnT, and CK-MB) and serum creatinine have been demonstrated to be

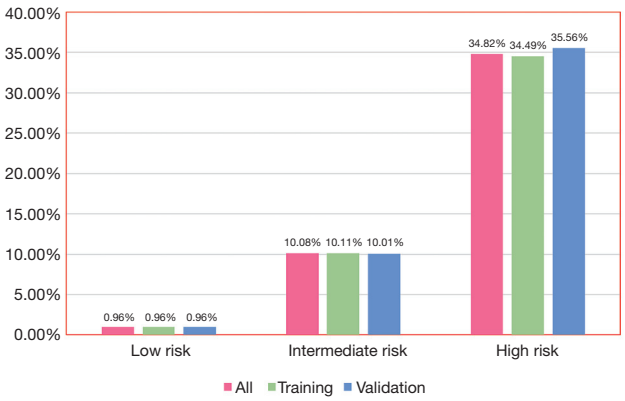

Figure 4 Observed incidence of in-hospital death. Observed incidence of in-hospital death according to categories of the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome risk score (CCC-ACS score) in the training and validation datasets. low risk (score ≤12), moderate risk (score: 13–20), and high risk (score ≥21).

independently associated with adverse outcomes (4,21,31,32), and can improve the discrimination ability of risk scores. However, these markers demand additional time and effort for blood tests to be performed; thus, they are usually not available during early medical contact. In fact, the data of cardiac markers and serum creatinine were lacking for a number of patients in the real-world registry used in the present study.

The main aim of this study was not to replace existing risk scores, but to establish a risk score with variables that are rapidly available at early medical contact. In the emergency unit, where it is busy and risk evaluation needs to be conducted promptly, a risk score based on readily available variables is practically more meaningful. This is also true for ambulance services, community health services, and other facilities with limited medical resources. Although it consists of rapidly obtainable variables, the CCC-ACS risk score displayed similar predictive ability for in-hospital death compared to the GRACE score. In addition, the CCC-ACS risk score exhibited good discrimination ability for those underwent PCI (AUC: 0.84), which is fitting of current clinical practice. Therefore, the CCC-ACS score may serve as a complement to previous risk scores.

There are potential applications of the CCC-ACS risk score. Firstly, stratifying patients at early medical contact without the need for blood tests may facilitate the quick identification of those with the highest risk and, subsequently, their quick and appropriate treatment. Secondly, some identified predictors in this model may provide useful information for updating other ACS risk scores.

Limitations

The present study has several limitations. Firstly, the rate of in-hospital mortality was relatively low among the patients in this study. One explanation was that phase I and phase II of the CCC-ACS project involved only tertiary hospitals, which exhibit a higher standard of patient care than other levels of hospitals. Furthermore, patients who died before or during transfer to the involved hospitals were not included in this study. Secondly, even though the CCC-ACS score was derived from a large-scale dataset, external validation is always required before its general application. Thirdly, the CCC-ACS project is a nationwide hospital-based quality improvement registry program without follow-up data. Therefore, whether the CCC-ACS risk score holds value for long-term prognosis is unknown. This question needs to be solved in further studies with follow-up. Finally, since the data in the CCC-ACS project were obtained from Chinese patients, further investigation is needed to determine whether the risk score performs as well in other populations.

Conclusions

The CCC-ACS CS score, which was developed from a large-scale dataset of unselected ACS patients, can quantify the risk of in-hospital death for patients with ACS at early medical contact and may facilitate clinical decision-making. However, further external validation of this risk score is required.

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Footnote

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