


# openheart Novel scoring system based on clinical examination for prediction of in-hospital mortality in acute coronary syndrome patients: a retrospective cohort study

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## ABSTRACT

**Background** This study aims to develop PADjadjaran Mortality in Acute coronary syndrome (PADMA) Score to predict in-hospital mortality in acute coronary syndrome (ACS) patients based on clinical examination only. Additionally, we also compared the predictive value of the PADMA Score with the Global Registry of Acute Coronary Events (GRACE), Canada Acute Coronary Syndrome (C-ACS), and The Portuguese Registry of Acute Coronary Syndromes (ProACS) risk scores.

**Methods** This retrospective cohort study included all ACS patients aged  $\geq 18$  years who were admitted to Dr. Hasan Sadikin Central General Hospital from January 2018 to January 2022. Patients' demographic, comorbidities and clinical presentation data were collected and analysed using multivariate logistic regression to create two models of scoring system (probability and cut-off model) to predict in-hospital all-cause mortality. The area under the curve (AUC) among PADMA, GRACE, C-ACS and ProACS risk scores was compared using the fisher Z test.

**Results** Multivariate regression analysis of 1359 patients showed that older age, history of cerebrovascular disease, tachycardia, high Shock Index and Killip class III and IV were independent mortality predictors and included in the PADMA Score. PADMA Score ranged from 0 to 20, with a score  $\geq 5$  that can predict all-cause mortality with 82.78% sensitivity and 72.35% specificity. The difference in AUC between PADMA and GRACE scores was insignificant ( $p=0.126$ ). Moreover, the AUC of the PADMA Score was significantly higher compared with the C-ACS ( $p=0.002$ ) and ProACS risk scores ( $p<0.001$ ).

**Conclusion** PADMA Score is a simple scoring system to predict in-hospital mortality in ACS patients. PADMA Score  $\geq 5$  showed an accurate discriminative capability to predict in-hospital mortality, comparable with the GRACE Score and superior to C-ACS and ProACS scores.

## INTRODUCTION

Cardiovascular diseases (CVD) are a global health burden and are responsible for one-third of mortality worldwide. In 2019, approximately 17.9 million people

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Although the Global Registry of Acute Coronary Events (GRACE) risk Score is the most widely used scoring system for predicting the risk of mortality in acute coronary syndrome (ACS) patients, this scoring system is time-consuming and cannot be performed in healthcare centres with limited facilities.

### WHAT THIS STUDY ADDS

⇒ This study develops a novel scoring system to predict the risk of in-hospital mortality in ACS patients based only on clinical examination, namely PADjadjaran Mortality in Acute coronary syndrome (PADMA) risk Score.  
⇒ The predictive value of the PADMA Score is proven to be comparable to the GRACE risk Score and superior to Canada Acute Coronary Syndrome and Portuguese Registry of Acute Coronary Syndromes scores.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Since the PADMA Score is simple and easy to calculate, clinicians can rapidly predict the risk of in-hospital mortality of ACS patients in the first medical contact.

died from CVD. Its prevalence is expected to increase.<sup>1</sup> Compared with other CVD, acute coronary syndrome (ACS) is a worldwide health issue with the highest mortality rate, with over three-quarters of CVD deaths in low-middle-income countries.<sup>1 2</sup> Therefore, the risk stratification tool to predict mortality risk in this population is mandatory to assess the early prognosis and help clinicians decide the best therapeutical options for the patients.

Until now, several prognostic tools (eg, Global Registry of Acute Coronary Events [GRACE], Thrombolysis in Myocardial

**Table 1** Baseline characteristic of the study participants

Variable	Total n=1359	Non-survivor n=151	Survivor n=1208	P value
Gender, n (%)				
Female	318 (23.4)	50 (33.1)	268 (22.2)	0.003*
Male	1041 (76.6)	101 (66.9)	940 (77.8)	
Age (years), mean±SD	58±11	64±12	57±11	<0.001*
Age (years) classifications, n (%)				
<65	991 (72.9)	74 (49)	917 (75.9)	<0.001*
65–75	263 (19.4)	45 (29.8)	218 (18)	
>75	105 (7.7)	32 (21.2)	73 (6)	
BMI (kg/m <sup>2</sup> ), mean±SD	24.3±3.5	23.9±3.6	24.4±3.5	0.209*
Obesity (BMI≥30 kg/m <sup>2</sup> )	92 (6.8)	9 (4)	86 (7.1)	0.147
Smoking, n (%)	812 (59.7)	75 (49.7)	737 (61.0)	0.007*
Diabetes melitus, n (%)	293 (21.6)	41 (27.2)	252 (20.9)	0.076
Hypertension, n (%)	854 (62.8)	100 (66.2)	754 (62.4)	0.361
Family history of CAD, n (%)	126 (9.3)	12 (7.9)	114 (9.4)	0.552
Cerebrovascular disease, n (%)	96 (7.1)	21 (13.9)	75 (6.2)	<0.001*
History of angina, n (%)	451 (33.2)	57 (37.7)	394 (32.6)	0.207
History of revascularisation, n (%)	181 (13.3)	17 (11.3)	164 (13.6)	0.429
SBP (mm Hg), mean±SD	121±25	108±30	123±23	<0.001*
SBP (mm Hg) classifications, n (%)				
≤100	319 (23.5)	69 (45.7)	250 (20.7)	<0.001*
>100	1040 (76.5)	82 (54.3)	958 (79.3)	
HR (bpm), mean±SD	82±19	93±25	81±18	<0.001*
HR (bpm) classifications, n (%)				
≤100	1169 (86.0)	93 (61.6)	1076 (89.1)	<0.001*
>100	190 (14.0)	58 (38.4)	132 (10.9)	
Shock Index†, mean±SD	0.71±0.32	0.93±0.36	0.68±0.30	<0.001*
Shock Index classifications, n (%)				
≤0.70	810 (59.6)	41 (27.2)	769 (63.7)	<0.001*
0.71–1.00	431 (31.7)	57 (37.7)	374 (31)	
>1.00	118 (8.7)	53 (35.1)	65 (5.4)	
ACS classifications, n (%)				
STEMI	801 (58.9)	103 (68.2)	698 (57.8)	0.014*
NSTEMI/UAP	558 (41.1)	48 (31.8)	510 (42.2)	
Killip class, n (%)				
I	965 (71.0)	52 (34.4)	913 (75.6)	<0.001*
II	218 (16.0)	24 (15.9)	194 (16.1)	
III	38 (2.8)	13 (8.6)	25 (2.1)	
IV	138 (10.2)	62 (41.1)	76 (6.3)	
Revascularisation procedures, n (%)				
PCI	733 (53.9)	62 (41.1)	671 (55.5)	<0.001*
Fibrinolytic	42 (3.1)	4 (2.6)	38 (3.1)	<0.001*
Pharmacological treatments, n (%)				
DAPT	1338 (98.5)	144 (95.8)	1194 (98.8)	0.006*
Anticoagulant	1321 (97.2)	142 (94.0)	1179 (97.6)	0.030*
ACE-I/ARB	833 (61.3)	31 (20.5)	802 (66.4)	<0.001*

Continued

**Table 1** Continued

Variable	Total n=1359	Non-survivor n=151	Survivor n=1208	P value
BB	986 (72.6)	34 (22.5)	952 (78.8)	<0.001*
Statin	1321 (97.2)	129 (85.4)	1192 (98.7)	<0.001*

All categorical data are presented in n (%).

All numerical data are presented in mean±SD.

\*Significant p value

†p<0.05, \*\*p<0.01, \*\*\*p<0.001.

†Shock Index is calculated by heart rate divided by systolic blood pressure.

ACE-I, ACE inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; BB, beta-blocker; BMI, body mass index; bpm, beat per minute; CAD, coronary artery disease; DAPT, dual antiplatelet; HR, heart rate; PCI, primary percutaneous intervention; SBP, systolic blood pressure.

Infarction [TIMI], Zwolle De Luca, Primary Angioplasty in Myocardial Infarction [PAMI] Addala and Cadillac Halkin) have been discovered to predict the risk of mortality in ACS patients.<sup>3</sup> Nonetheless, GRACE Score is still the most widely used scoring system and also the validated instruments that had the highest sensitivity and specificity in predicting mortality compared with other prognostic tools.<sup>4-5</sup> However, this scoring system relies heavily on electrocardiography (ECG) and laboratory findings to complete the calculation; hence, it is time-consuming and cannot be performed in rural healthcare centres with limited facilities.

Several cohort studies evaluate the usefulness of the CHA<sub>2</sub>DS<sub>2</sub>VASc (Congestive heart failure, Hypertension, Aged ≥ 75 years, Diabetes mellitus, Stroke, Vascular disease, Aged 65-74 years, Sex category [female]) score as a clinical scoring system in which the calculation is based only on the history of a patient's comorbidities.<sup>6-8</sup> These cohort studies showed that a high CHA<sub>2</sub>DS<sub>2</sub>VASc Score significantly increased the risk of major adverse cardiac events in ACS patients regardless of atrial fibrillation status.<sup>6-8</sup> Nevertheless, although this scoring system is convenient compared with the GRACE Score, it also has limitations as it does not include the patient's clinical presentation into the calculation; therefore, it can underestimate the mortality risk in ACS patients with poor haemodynamic status. Thus, this study aims to develop a novel risk scoring system named PADjajaran Mortality in Acute coronary syndrome (PADMA) Score to predict the risk of in-hospital mortality in ACS patients, which in the calculation is based on the patient's history and clinical presentation at admission. This scoring is simple and can be completed in the first medical contact in all healthcare facilities. Additionally, we also compared the prognostic value of the PADMA Score with other scoring systems, including GRACE, Canada Acute Coronary Syndrome (C-ACS) and The Portuguese Registry of Acute Coronary Syndromes (ProACS) risk scores.

## METHODS

### Study design and patient selection

This retrospective and single-centre cohort study included all ACS patients aged ≥18 years hospitalised in Dr. Hasan Sadikin Central General Hospital from January 2018 to January 2022. Incomplete or missing data from medical records were excluded from the study.

### Definition of variables and outcome

Variables that were considered in the model were as follows; demography (female sex, age, body mass index (BMI)), clinical presentation (initial systolic blood pressure (SBP), initial heart rate (HR), Shock Index (SI), which is defined as HR divided by SBP, Killip class and ST-segment deviation in ECG), history and cardiovascular risk factors (smoking, diabetes, hypertension, family history of coronary artery disease, history of cerebrovascular disease, history of angina and history of revascularisation, including primary percutaneous intervention and coronary artery bypass surgery). All these variables were collected from the patient's medical records. The primary endpoint was in-hospital mortality, defined as all-cause death that occurred during the index hospitalisation of the ACS event.

### Statistical analyses

All statistical analyses were performed using SPSS V.25.0. All categorical data were presented in numbers and percentages. In contrast, numerical data were presented in mean and SD if the distribution was normal or median and IQR if the distribution was not normal. Chi-square and Fisher's tests were performed to analyse the association between predicting factors and in-hospital mortality. The logistic regression analysis was performed to find the significant p value (p<0.05) from the adjusted OR. All the significant parameters were included in logistic regression with a stepwise backward method. The scoring system was developed by numbering each independent variable based on the regression coefficient (B) from multivariate logistic regression analysis. Receiver operating characteristics (ROC) analysis was used to produce the area under the curve (AUC) for predicting the outcome of interest. Moreover, the DeLong method was used to generate the

**Table 2** Logistic regression analysis of in-hospital mortality risk

Variable	Crude OR (95% CI)	P value	AOR (95% CI)	P value
Gender				
Female	1.736 (1.205 to 2.501)	0.003*	1.389 (0.84 to 2.295)	0.200
Male	1 (ref)		1 (ref)	
Age (years)				
<65	1 (ref)		1 (ref)	
65–75	2.558 (1.717 to 3.812)	<0.001*	2.437 (1.53 to 3.884)	<0001*
>75	5.432 (3.367 to 8.764)	<0.001*	4.042 (2.225 to 7.344)	<0001*
Obesity (BMI>30 kg/m <sup>2</sup> )	0.540 (0.232 to 1.257)	0.153	0.705 (0.275 to 1.809)	0.468
Smoking	0.631 (0.449 to 0.885)	0.007*	0.945 (0.587 to 1.52)	0.814
Diabetes melitus	1.414 (0.963 to 2.077)	0.076	1.139 (0.719 to 1.804)	0.580
Hypertension	1.181 (0.826 to 1.687)	0.361	1.321 (0.85 to 2.053)	0.216
Family history of CAD	0.828 (0.445 to 1.541)	0.552	1.03 (0.494 to 2.147)	0.936
History of cerebrovascular disease	2.440 (1.455 to 4.092)	<0.001*	1.954 (1.032 to 3.698)	0.040*
History of angina	1.253 (0.883 to 1.778)	0.207	1.551 (0.972 to 2.475)	0.066
History of revascularisation	0.808 (0.475 to 1.373)	0.429	0.791 (0.398 to 1.573)	0.505
SBP (mm Hg)				
≤100	3.224 (2.274 to 4.572)	<0.001*	0.963 (0.558 to 1.661)	0.892
>100	1 (ref)		1 (ref)	
HR (beat/min)				
≤100	1 (ref)		1 (ref)	
>100	5.084 (3.496 to 7.393)	<0.001*	1.859 (1.08 to 3.202)	0.025*
Shock Index†				
≤0.70	1 (ref)		1 (ref)	
0.71–1.00	2.859 (1.878 to 4.350)	<0.001*	2.189 (1.341 to 3.572)	0.002*
>1.00	15.293 (9.465 to 24.712)	<0.001*	4.033 (1.844 to 8.82)	<0.001*
ACS				
STEMI	1.568 (1.093 to 2.250)	0.015*	1.367 (0.879 to 2.125)	0.166
NSTEMI/UAP	1 (ref)		1 (ref)	
Killip class				
I	1 (ref)		1 (ref)	
II	2.172 (1.307 to 3.610)	0.003*	1.244 (0.711 to 2.176)	0.445
III	9.130 (4.417 to 18.872)	<0.001*	4.768 (2.07 to 10.98)	<0.001*
IV	14.323 (9.257 to 22.164)	<0.001*	6.859 (3.933 to 11.963)	<0.001*

\*Significant p value

\*\*p&lt;0.05, \*\*p&lt;0.01, \*\*\*p&lt;0.001.

†Shock Index is calculated by heart rate divided by systolic blood pressure.

AOR, adjusted OR; BMI, body mass index; CAD, coronary artery disease; HR, heart rate; NSTEMI, non-ST segment elevation myocardial infarction; SBP, systolic blood pressure; STEMI, ST-elevation myocardial infarction; UAP, unstable angina pectoris.

PADMA Score's sensitivity and specificity and determine the ideal cut-off. The Granger model was performed to obtain the estimated probability of mortality for in-hospital death. The scoring system validated the previous sample to find diagnostic value. Finally, to compare the prognostic value of PADMA, GRACE, C-ACS and ProACS risk scores, we compared the AUC of these scoring systems using Fisher Z test.

## RESULTS

The baseline characteristics of the studies are summarised in [table 1](#). Of 1359 subjects who enrolled in this study, most of the patients were male (76.6%) and less than 65 years (72.9%). Most patients were non-obese (6.8%), more than half of the subjects were smokers (59.7%) and had hypertension (62.8%). The initial presentation showed that most of the patients had no

**Table 3** Assessment of the score value from each independent predictor factor

Variable	B	SE	B/SE	$\frac{(B/SE)}{\text{lowest } (B/SE)}$	Score
Age (years)					
<65 (ref)					
65–75	0.923	0.232	3.98	3.92	4
>75	1.458	0.290	5.03	4.96	5
History of cerebrovascular disease					
	0.703	0.321	2.19	2.16	2
Heart rate (beat per minute)					
≤100 (ref)					
>100	0.623	0.266	2.34	2.31	2
Shock Index*					
≤0.70 (ref)					
0.71–1.00	0.767	0.238	3.22	3.18	3
>1.00	1.392	0.345	4.03	3.98	4
Killip class					
I (ref)					
II	0.284	0.280	1.01	1.00	1
III	1.718	0.415	4.14	4.08	4
IV	1.913	0.265	7.22	7.12	7

\*Shock Index is calculated by heart rate divided by systolic blood pressure.

congestion (71%) with stable haemodynamics with HR less than 100 bpm (86%), blood pressure more than 100 mm Hg (76.5%) and SI less than 0.7 (59.6%). More than half of the ECG presented ST elevation (58.9%).

In-hospital mortality occurred in 151 patients (11.1%). Female gender, older age, smoking and patients who had a history of cerebrovascular disease, low SBP, increased HR, high SI, ST-segment elevation myocardial infarction (STEMI) and high Killip class (III and IV) were significantly associated with higher mortality risk ( $p<0.05$ ). Furthermore, the survivors had a higher number of revascularisation procedures and medical treatments in opposition to the non-survivors ( $p<0.05$ ).

Table 2 showed the bivariate and multivariate regression analyses. Independence predictor in mortality were age 65–75 years (AOR=2.437 (95% CI=1.530 to 3.884);  $p<0.001$ ), age>75 years (AOR=4.042 (95% CI=2.225 to 7.344);  $p<0.001$ ), history of cerebrovascular disease (AOR=1.954 (95% CI=1.032 to 3.698);  $p=0.04$ ), HR>100 bpm (AOR=1.859 (95% CI=1.080 to 3.202);  $p=0.025$ ), SI 0.71–1.00 (AOR=2.189 (95% CI=1.341 to 3.572);  $p=0.002$ ), SI>1.00 (OR=4.033 (95% CI=1.844 to 8.820);  $p<0.001$ ), Killip III (OR=4.768 (95% CI=2.07 to 10.98);  $p<0.001$ ) and Killip IV (OR=6.859 (95% CI=3.933 to 11.963);  $p<0.001$ ).

Several independent predictors that were calculated as a new scoring system were elaborated in table 3. The

**Table 4** Scoring system based on patient's probability on mortality event

Scoring	Probability (%)
0	2.2
1	3.0
2	3.9
3	5.2
4	6.8
5	9.0
6	11.7
7	15.1
8	19.2
9	24.2
10	30.0
11	36.5
12	43.6
13	50.9
14	58.2
15	65.1
16	71.5
17	77.1
18	81.8
19	85.8
20	89.0

scoring result is based on regression coefficient (B) from multivariate logistic regression with a minimum score of 0 and the maximum score of +20. It showed that the lowest score is Killip II with 1 point, history of cerebrovascular disease and HR got 2 points, SI 0.7–1.0 got 3 points, age 65–75, SI>1.00 and Killip III got 4 points, age>75 years got 5 points and the highest score is Killip IV with 7 points.

Table 4 shows the scoring model based on the probability of mortality events—the greater the score, the higher chance of mortality, which indicates a dose-response related. ROC analysis revealed that with a cut-off of 5, the AUC, sensitivity and specificity of this scoring system in predicting in-hospital mortality were 0.842, 82.78% and 72.35%, respectively, (table 5 and figure 1).

Furthermore, we performed the Granger model to predict the incidence of mortality events based on three risk categories of PADMA Score (low risk: 0, moderate risk: 1–4 and high risk: 5–20). This model showed that low, intermediate and high risk yielded a probability of death of <3.0%, 3.0–6.8% and >6.8%, respectively, and an accumulated patient of 457 (33.6%), 463 (34%) and 440 (32.4%), respectively, (table 6).

We compared the predictive value of the PADMA Score with the GRACE, C-ACS and ProACS scores using the Fisher Z test. The AUC value between PADMA and GRACE risk scores was not statistically significant for predicting in-hospital mortality ( $p=0.126$ ). Furthermore,



**Table 5** Receiver operating characteristics (ROC) analysis as mortality scoring system model

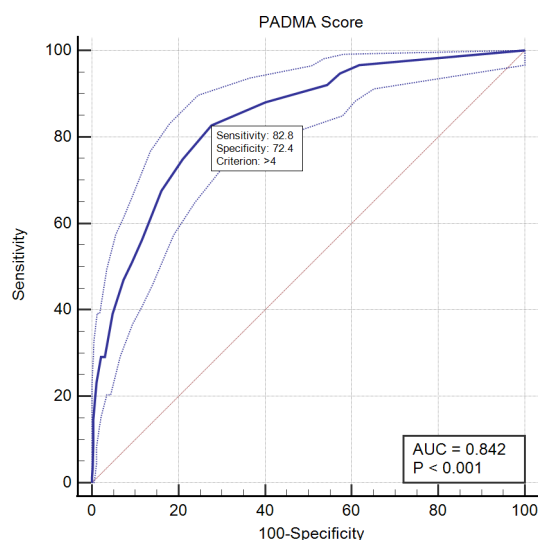
Variable	AUC (95% CI)	P value	Cut-off value	Diagnostic value
Score	0.842 (0.821 to 0.861)	<0.001	≥5	Sensitivity: 82.78%
				Specificity: 72.35%
				PPV: 27.2%
				NPV: 97.1%
				LR+: 2.99
				LR-: 0.24

NPV, negative predictive value; AUC, area under curve; LR, likelihood ratio; PPV, positive predictive value.

it showed that the AUC value of the PADMA Score was significantly higher in comparison to C-ACS ( $p=0.002$ ) and ProACS risk scores ( $p<0.001$ ) (table 7 and figure 2).

## DISCUSSION

The major findings of this cohort study are as follows. First, the components of the PADMA Score were age, history of cerebrovascular disease, HR, SI and Killip class. Second, the association between PADMA scores and in-hospital mortality in ACS patients showed that every increment of one score presented a higher mortality risk. PADMA Score was classified into three risk stratification: low, intermediate and high, with the probability of in-hospital mortality being <3%, 3%–6.8% and >6.8%, respectively. Third, using the cut-off of 5, a high PADMA Score substantially increased the risk of in-hospital mortality with AUC, sensitivity and specificity were 0.842, 82.78%, and 72.35%, respectively. Fourth, the PADMA Score's predictive value was comparable to the GRACE Score and superior to the C-ACS and ProACS scores in predicting the risk of in-hospital mortality in ACS patients. Thus, we recommended using the PADMA Score as a simple prognosticator of in-hospital mortality in ACS patients.



**Figure 1** Receiver operating characteristics curve score to predict mortality. AUC, area under the curve; PADMA, PADjadjaran Mortality in Acute coronary syndrome.

There are two similar scoring systems to ours that only require a clinical examination to complete the calculation: C-ACS and ProACS risk scores. The C-ACS and ProACS were initiated in Canada and Portuguese, respectively.<sup>9 10</sup> In this study, the PADMA Score was superior in predicting in-hospital mortality compared with C-ACS and ProACS scores based on the AUC values. According to the C-ACS and ProACS development cohorts, these two scoring systems had significantly lower AUC values than the GRACE risk Score.<sup>9 10</sup> Otherwise, the predictive value of the PADMA Score was shown to be comparable with the GRACE Score, indicating that the PADMA Score can be useful as an alternative scoring system to the GRACE risk Score. However, there are several differences in baseline characteristics between this study and other cohorts. In contrast to GRACE, C-ACS and ProACS cohorts, patients in our study were younger, had fewer females and incidences of diabetes mellitus and history of angina, but had higher smokers, STEMI, and Killip class IV presentation.<sup>11–13</sup> In addition, our patients had lower SBP and BMI levels than other cohorts. Moreover, as opposed to the ProACS development cohort, the revascularisation procedures in this study were higher.<sup>10</sup> The in-hospital mortality rate in GRACE, C-ACS and ProACS cohorts were 4%, 5.2% and 5.4%, respectively, in which these numbers are approximately half of the mortality rate in our study.<sup>9 10 13</sup> The possible explanation for this phenomenon is that compared with other cohorts, our study had a higher number of STEMI patients and Killip class IV presentation, thereby significantly increasing the risk of in-hospital mortality.

Generally, the PADMA Score encompasses two main elements, including demographic and haemodynamic

**Table 6** PADMA scoring system based on patient's probability on mortality event

Risk category (tertiles)	PADMA Score	Probability of death
Low	0	<3.0
Intermediate	1–4	3.0–6.8
High	5–20	>6.8

PADMA, PADjadjaran Mortality in Acute coronary syndrome.

**Table 7** ROC analysis result between GRACE and PADMA scoring system based on mortality

Variable	AUC (95% CI)	AUC difference (95% CI)	P value
PADMA Score	0.842 (0.821 to 0.861)	Ref	
GRACE Score	0.863 (0.843 to 0.881)	0.021 (−0.006 to 0.048)	0.126
C-ACS	0.798 (0.775 to 0.819)	0.042 (0.017 to 0.071)	0.002*
ProACS	0.760 (0.737 to 0.783)	0.082 (0.049 to 0.115)	<0.001*

\*Significant p value

AUC, area under curve; C-ACS, Canada Acute Coronary Syndrome; GRACE, Global Registry of Acute Coronary Events; PADMA, PADjadjaran Mortality in Acute coronary syndrome; ProACS, The Portuguese Registry of Acute Coronary Syndromes; ROC, receiver operating characteristics.

status at admission. Demographic status is represented by age and history of cerebrovascular disease. Whereas HR, SI and Killip class reflect haemodynamic status. Every component of this scoring system was statistically significant and independent in increasing mortality in ACS patients and relatively reasonable to be included, given that every component had its mechanism related to mortality.

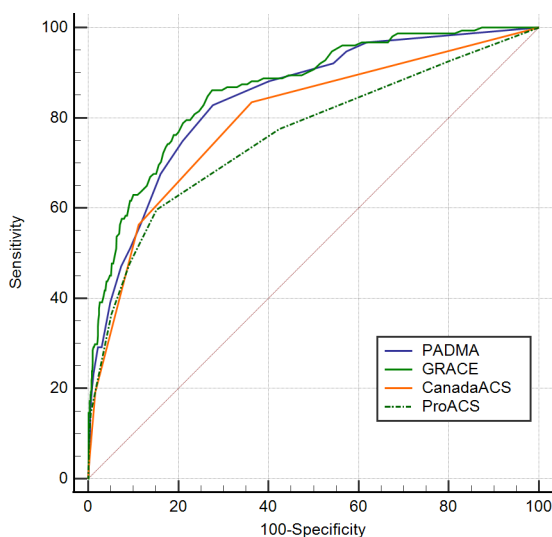
According to the current study, older age was one of the independent predictors of mortality, with age 65–75 and >75 years had 2.5 times and 4 times, respectively, higher mortality risk compared with those with age <65 years. Consistently, previous two cohort studies stated that old patients (>65 years and >75 years) significantly increased the risk of mortality in ACS patients.<sup>14 15</sup> Furthermore, there are several explanations for why old ACS patients tend to present with high mortality risk. First, older patients are more likely to have comorbidities such as kidney disorders and hypertension.<sup>16</sup> Second, mostly old patients who were finally diagnosed with ACS were

presented with atypical symptoms at admission, often getting delayed diagnosis and treatment. Third, since old patients have a higher risk of bleeding, several old patients are not tolerable to undergo revascularisation procedures according to guidelines.<sup>17</sup>

This study showed that a history of cerebrovascular disease had a significant effect on mortality in ACS patients, which this variable was not used in GRACE or TIMI scores.<sup>18 19</sup> Consistent with our findings, the association between cerebrovascular disease in the ACS population and mortality has been revealed by Mukherjee *et al.*<sup>20</sup> Furthermore, patients with the cerebrovascular disease were less likely to be treated invasively or had limited medical drugs.<sup>21</sup> Additionally, when coronary angiography was performed, patients with prior cerebrovascular disease often had multivessel disease, which increased the risk of death.<sup>22</sup>

Another novel and interesting finding in our study, we include the SI as a parameter in this study. The SI comprises two main components: HR and SBP. Originally, this index was used in patients who experienced hypovolemic and haemorrhagic shock.<sup>23</sup> Nonetheless, several studies proved that high SI was significantly correlated with higher mortality risk in ACS populations.<sup>24–29</sup> In this study, we divided SI into three categories, including <0.70, 0.71–1.00 and >1.00. This study showed that those with moderate (0.71–1.00) and high SI (>1.00) significantly and independently increased the risk of mortality by two times and four times higher as opposed to patients with low SI (<0.7). This finding is aligned with several cohort studies results, which revealed that SI higher than 0.7 and 1 significantly elevated the risk of mortality in ACS patients.<sup>24–29</sup>

In this study, high HR (>100) at admission was associated with increased mortality by approximately two times higher in contrast to those with low HR (<100). Consistently, previous studies supporting this result revealed that high admission HR was independently linked to mortality in ACS patients.<sup>9 15 30–32</sup> It is widely known that sympathetic hyperactivity caused by a catecholamine surge in ACS patients can increase the HR. A study by Petterson *et al* found that high catecholamine levels in ACS patients were correlated with low left ventricular ejection fraction (LVEF).<sup>33</sup> Moreover, sympathetic stimulation in ACS



**Figure 2** Comparison of AUC of PADMA Score with GRACE, C-ACS and ProACS risk scores to predict in-hospital mortality. AUC, area under curve; C-ACS, Canada Acute Coronary Syndrome; GRACE, Global Registry of Acute Coronary Events; PADMA, PADjadjaran Mortality in Acute coronary syndrome; ProACS, The Portuguese Registry of Acute Coronary Syndromes.

patients can cause ischemia-induced ventricular fibrillation and lead to sudden cardiac death.<sup>34</sup> In addition, Yuksek *et al* stated that ACS patients who presented with elevated HR had higher serum troponin, glucose levels, lower LVEF and were more likely to have acute heart failure.<sup>35</sup>

An observational study conducted by Shlomai *et al* stated that admission SBP in ACS patients had a predictive value on mortality, as those with low SBP had a significant mortality risk compared with those with normal SBP.<sup>36</sup> On the contrary, our study demonstrated that blood pressure less than 100 mm Hg was not significantly increased the risk of mortality in multivariate analysis. However, when SBP is included in the calculation of SI, the significance was numerically obtained. Theoretically, low SBP reflects low mean arterial pressure, as patients with low SBP, can lead to end-organ hypoperfusion and death.<sup>37 38</sup> Thus, it concludes that ACS patients with high HR and low SBP indicated by high SI were associated with reduced LV function, increased arrhythmia risk and induced end-organ damage, leading to elevated mortality risk.

Our last PADMA Score component is the Killip class which is the standard classification to predict mortality in myocardial infarction. The higher Killip class was linked with a higher risk of in-hospital mortality.<sup>39</sup> Persistently, the current study revealed that Killip class III and IV were independently associated with higher mortality risk. Basically, the Killip class is determined by pre-existing heart failure conditions (acute or chronic) and cardiogenic shock status. Heart failure markedly increased mortality risk in ACS patients, as it reduced the cardiac output, diminished the oxygen perfusion into the lung circulatory and induced renin–angiotensin–aldosterone system activation.<sup>40</sup> On the other hand, cardiogenic shock, as an indicator of end-organ hypoperfusion due to cardiac dysfunction, significantly increased the risk of mortality in ACS patients.<sup>41 42</sup>

This study has several limitations. First, this study had a relatively small sample size and was only conducted in a single centre. Second, according to its retrospective design, it can lead to recall and selection bias. Third, due to the high amount of loss to follow-up, this scoring is limited to predicting only in-hospital mortality. Last, to better evaluate the association between PADMA Score and mortality in ACS patients, this scoring system still needs further validation by a multicentre cohort study with numerous participants and a longer duration of follow-up.

## CONCLUSION

In conclusion, this study proudly presented the new scoring system to predict in-hospital mortality in ACS patients, PADMA Score, with several components including age, history of cerebrovascular disease, HR, SI and Killip class. This study revealed that the association between PADMA Score and in-hospital mortality was dose–response related. Moreover, this scoring system

showed a good predictive value for predicting in-hospital mortality, which was comparable to the GRACE Score and superior to C-ACS and ProACS risk scores. Therefore, we highly suggest using the PADMA Score as a convenient scoring system for all ACS patients in an emergency setting to predict the risk of in-hospital mortality.

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