

The AHEAD score as a predictor of all-cause mortality in patients with acute myocardial infarction: a secondary analysis of the Japan Acute Myocardial Infarction Registry



Mike Saji^{1,2*}, MD; Satoshi Honda³, MD; Kensaku Nishihira⁴, MD; Sunao Kojima⁵, MD; Misa Takegami^{6,7}, MD; Yasuhide Asaumi³, MD; Jun Yamashita⁸, MD; Kiyoshi Hibi⁹, MD; Jun Takahashi¹⁰, MD; Yasuhiko Sakata³, MD; Morimasa Takayama¹, MD; Tetsuya Sumiyoshi¹, MD; Hisao Ogawa¹¹, MD; Kazuo Kimura¹², MD; Satoshi Yasuda¹⁰, MD; on behalf of the JAMIR investigators

*Corresponding author: Department of Cardiology, Sakakibara Heart Institute, 3-16-1, Asabicho, Tokyo, 183-0003, Japan.
E-mail: mikesaji8@gmail.com

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ABSTRACT

BACKGROUND: The AHEAD score – comprising atrial fibrillation, haemoglobin, elderly age, abnormal renal function, and diabetes mellitus – is a validated prognostic model for patients with heart failure. However, its predictive value in acute myocardial infarction (MI), particularly in large real-world cohorts, remains uncertain.

AIMS: We aimed to assess the utility of the AHEAD score in predicting 1-year all-cause mortality in patients with acute MI.

METHODS: This secondary analysis of the Japan Acute Myocardial Infarction Registry (JAMIR) included 3,067 patients with acute MI enrolled across 50 Japanese institutions between December 2015 and May 2017. Patients were stratified by AHEAD score at admission. The primary endpoint was all-cause mortality within 1 year after acute MI. Multivariable Cox regression, Kaplan-Meier survival analysis, and restricted cubic spline modelling were used to evaluate the association between the AHEAD score and mortality.

RESULTS: Higher AHEAD scores were associated with older age, more comorbidities, a higher Killip class, and delayed reperfusion. The 1-year all-cause mortality rate increased significantly with rising AHEAD scores. The AHEAD score was an independent predictor of all-cause mortality (adjusted hazard ratio 1.60; 95% confidence interval: 1.39-1.84; $p < 0.001$), and this association was consistent across predefined subgroups. Spline analysis demonstrated a linear relationship between the AHEAD score and the mortality risk.

CONCLUSIONS: The AHEAD score is a simple, bedside-accessible tool that effectively predicts 1-year all-cause mortality in patients with acute MI, regardless of the presence of heart failure. Its use may aid early risk stratification and guide clinical decision-making in acute cardiovascular care. This study was registered with the Japanese UMIN Clinical Trials Registry (UMIN000019479).

KEYWORDS: acute coronary syndrome; acute heart failure; predictive model

Heart failure (HF) accounts for an increasing proportion of heart disease cases in ageing populations worldwide, with particularly poor treatment outcomes observed in Asia^{1,2}. As HF is associated with high morbidity and mortality, an effective prediction scheme is urgently needed to identify patients at risk of adverse events, which would facilitate the development of preventive strategies. The AHEAD score (A: atrial fibrillation; H: haemoglobin; E: elderly; A: abnormal renal parameters; D: diabetes mellitus), a simple bedside clinical prognostic model that has been validated in both European and Asian populations, has been widely used to predict all-cause mortality in patients with HF^{3,4}.

Due to the high success rate of primary percutaneous coronary intervention (PCI) and the increasing availability of ambulance services in Japan, in-hospital mortality has declined among patients with acute myocardial infarction (MI) in recent decades^{5,6}. In particular, the combination of primary PCI with drug-eluting stents and antithrombotic therapies, including P2Y₁₂ receptor inhibitors, has contributed to reductions in stent thrombosis and bleeding events. Moreover, the introduction of novel mechanical support devices has decreased the rate of periprocedural mechanical complications, resulting in more stable haemodynamics and shorter hospital stays following acute MI⁷⁻¹⁰. However, clinical outcomes remain poor in patients with severe acute HF⁵.

Although the AHEAD scoring system is known to be useful in patients with acute HF, limited data are available regarding its prognostic utility in large cohorts of patients with acute MI. Therefore, the aim of this study was to investigate whether the AHEAD score, as a surrogate marker of HF, could predict all-cause mortality – particularly in patients with acute MI, regardless of the presence or absence of acute HF.

Methods

STUDY POPULATION AND DESIGN

The Japan Acute Myocardial Infarction Registry (JAMIR) has been described in detail previously^{11,12}. Briefly, the JAMIR is a multicentre, nationwide, prospective registry in which consecutive patients with spontaneous onset of acute MI were enrolled at 50 institutions between December 2015 and May 2017. The diagnosis of acute MI was made based on either the Universal Definition of MI or the Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) criteria^{13,14}.

The following patients were excluded from the present secondary analysis: those admitted ≥ 24 hours after symptom onset, those with no return of spontaneous circulation on admission after out-of-hospital cardiopulmonary arrest, and those with acute MI occurring as a complication of PCI or coronary artery bypass grafting. Patient management was at the discretion of the treating physician.

Primary data – including patient demographics and outcomes – were collected from medical records. Data were

Impact on daily practice

The AHEAD score, a simple bedside tool, enables rapid risk stratification for patients with acute myocardial infarction. This study confirms its predictive value for 1-year all-cause mortality, even in patients without overt heart failure. Clinicians can apply the score at admission to identify high-risk patients, guide therapeutic decisions, and prioritise monitoring. Its simplicity allows for easy integration into clinical workflows and electronic health records. By enhancing early prognostic evaluation, the AHEAD score supports personalised care strategies, improves communication with patients and families, and contributes to more effective allocation of healthcare resources.

entered into the JAMIR system by investigators, clinical research coordinators, and local data managers at each site. Follow-up data at 1 year after MI onset were obtained using medical records from each institution. When follow-up data were unavailable due to reasons such as hospital transfer, a letter was sent to the patient requesting updated information. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The research protocol was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center as well as by the respective ethics committees or institutional review boards of all participating sites. Although informed consent was not obtained because of the observational design of the registry, an opt-out process was implemented through each institution's website and onsite postings, informing patients of the study and giving them the opportunity to decline participation in the JAMIR. The research secretariat also confirmed that the opt-out procedures were followed at each study site. The JAMIR study was registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN000019479). This secondary analysis was conducted using data on recorded patient characteristics, procedural details, and clinical outcomes. The primary endpoint of this study was all-cause mortality within 1 year following hospitalisation for acute MI.

STATISTICAL ANALYSIS

Continuous variables are presented as means $\pm$ standard deviations or medians with interquartile ranges, and categorical variables are expressed as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro-Wilk test. Statistical significance was defined as a two-sided p -value <0.05 . For continuous variables with normal distributions, comparisons were made using analysis of variance; for non-normally distributed variables, the Kruskal-Wallis test was used. Categorical variables were compared using the chi-squared test, as

Abbreviations

CK	creatinine kinase	LVEF	left ventricular ejection fraction	STEMI	ST-segment elevation myocardial infarction
DTB	door-to-balloon time	MI	myocardial infarction	TIMI	Thrombolysis in Myocardial Infarction
HF	heart failure	PCI	percutaneous coronary intervention		

appropriate. Cox proportional hazard regression analysis was performed to examine the association between the AHEAD score and all-cause mortality up to 1 year after discharge. Variables with p -values < 0.15 in the univariate analysis (**Table 1**) were included in the multivariate models. The individual components of the AHEAD score (i.e., atrial fibrillation, haemoglobin concentration, age, serum creatinine, and diabetes mellitus) were not included in the models to avoid multicollinearity. In sensitivity analyses, variables related to medical therapy were added to the multivariate model. Kaplan-Meier survival analysis and the log-rank test were used to estimate and compare cumulative mortality rates. A forest plot was generated to assess the association between the AHEAD score and all-cause mortality in predefined subgroups of patients with acute MI. A restricted cubic spline Cox regression model was used to evaluate the continuous relationship between the AHEAD score and all-cause mortality. The median AHEAD score of 1 was used as the reference point (hazard ratio 1.0). All analyses were

conducted using SPSS, version 26.0 (IBM) and R, version 4.4.1 (R Foundation for Statistical Computing).

Results

A total of 3,411 patients were registered in the JAMIR. Among them, we excluded patients with insufficient data: 7 lacked haemoglobin values, 9 lacked creatinine values, 221 were missing door-to-device time, 104 were missing final Thrombolysis in Myocardial Infarction (TIMI) flow data, and 3 lacked peak creatine kinase values. The final analysis included 3,067 patients (**Supplementary Figure 1**).

Table 1 presents the baseline characteristics of the study population. Patients with higher AHEAD scores were more likely to have hypertension, diabetes mellitus, peripheral artery disease, prior stroke, atrial fibrillation, ST-segment elevation MI (STEMI), and a higher Killip classification. They also had lower haemoglobin concentrations and estimated glomerular filtration rates and were less likely to have a door-to-device time of < 90 minutes. **Table 2** provides the angiographic and

Table 1. Baseline patient characteristics.

	AHEAD score (n=3,067)						<i>p</i> -value
	0 (n=931)	1 (n=1,082)	2 (n=650)	3 (n=314)	4 (n=77)	5 (n=13)	
Age, years	59 (51, 66)	68 (59, 76)	77 (72, 83)	80 (74, 85)	80 (75, 84)	77 (74, 80)	< 0.001
Male	825 (88.6)	837 (77.4)	431 (66.3)	211 (67.2)	53 (68.8)	11 (84.6)	< 0.001
Hypertension	584 (62.7)	784 (72.5)	494 (76.0)	251 (79.9)	71 (92.2)	12 (92.3)	< 0.001
Diabetes mellitus	0 (0)	447 (41.3)	316 (48.6)	221 (70.4)	64 (83.1)	13 (100)	< 0.001
Dyslipidaemia	670 (72.0)	766 (70.8)	424 (65.2)	204 (65.0)	47 (61.0)	10 (76.9)	0.011
Peripheral artery disease	8 (0.9)	31 (2.9)	36 (5.5)	25 (8.0)	10 (13.0)	3 (23.1)	< 0.001
Atrial fibrillation	0 (0)	26 (2.4)	56 (8.6)	72 (22.9)	34 (44.2)	13 (100)	< 0.001
Prior MI	49 (5.3)	91 (8.4)	69 (10.6)	47 (15.0)	31 (40.3)	3 (23.1)	< 0.001
Prior CABG	7 (0.8)	20 (1.8)	15 (2.3)	18 (5.7)	12 (15.6)	1 (7.7)	< 0.001
Prior stroke	30 (3.2)	96 (8.9)	81 (12.5)	59 (18.8)	17 (22.1)	4 (30.8)	< 0.001
Atrial fibrillation	0 (0)	26 (2.4)	56 (8.6)	72 (22.9)	34 (44.2)	13 (100)	< 0.001
Malignancy	31 (3.3)	83 (7.7)	75 (11.5)	48 (15.3)	18 (23.4)	2 (15.4)	< 0.001
STEMI	154 (16.5)	205 (18.9)	135 (20.8)	74 (23.6)	19 (24.7)	6 (46.2)	0.005
Killip classification							
I	803 (86.3)	884 (81.7)	462 (71.1)	181 (57.6)	41 (53.2)	5 (38.5)	< 0.001
II	55 (5.9)	77 (7.1)	72 (11.1)	45 (14.3)	9 (11.7)	2 (15.4)	-
III	25 (2.7)	43 (4.0)	30 (4.6)	40 (12.7)	12 (15.6)	4 (30.8)	-
IV	48 (5.2)	78 (7.2)	86 (13.2)	48 (15.3)	15 (19.5)	2 (15.4)	-
Haemoglobin, g/dL	15.1 (14.2, 16.0)	14.4 (13.3, 15.5)	12.8 (11.5, 14.3)	11.7 (10.5, 12.6)	11.3 (10.2, 11.9)	10.4 (8.6, 11.4)	< 0.001
eGFR, mL/min/1.73 m ²	73.5 (63.5, 85.2)	67.8 (54.6, 82.2)	58.2 (43.9, 72.6)	43.7 (27.3, 60.6)	22.7 (11.4, 31.8)	15.5 (6.96, 30.7)	< 0.001
LVEF, %	53 (46, 60)	53 (45, 60)	50 (42, 60)	50 (40, 60)	41 (30, 57)	44 (36, 55)	< 0.001
Door-to-balloon time < 90 min	685 (73.6)	772 (71.3)	437 (67.2)	196 (62.4)	46 (59.7)	6 (46.2)	< 0.001
Final TIMI flow=3	862 (92.6)	1,003 (92.7)	601 (92.5)	275 (87.6)	74 (96.1)	12 (92.3)	0.042
Peak CK concentration, IU/L	1,978 (878, 3,887)	1,750 (678, 3,627)	1,433 (546, 3,005)	1,135 (395, 3,015)	1,312 (446, 2,521)	1,286 (486, 2,580)	0.001

Values are presented as medians (interquartile ranges) or n (%). CABG: coronary artery bypass grafting; CK: creatine kinase; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; MI: myocardial infarction; STEMI: ST-segment elevation myocardial infarction; TIMI: Thrombolysis in Myocardial Infarction

Table 2. In-hospital outcomes and medical therapy during hospitalisation.

	AHEAD score (n=3,067)						p-value
	0 (n=931)	1 (n=1,082)	2 (n=650)	3 (n=314)	4 (n=77)	5 (n=13)	
Culprit lesion – left main	10 (1.0)	22 (2.0)	18 (2.7)	11 (3.5)	0 (0)	0 (0)	0.041
Culprit lesion – left anterior descending	487 (52.3)	537 (49.6)	300 (46.1)	133 (42.3)	32 (41.5)	8 (61.5)	0.013
Culprit lesion – left circumflex	130 (13.9)	164 (15.1)	109 (16.7)	46 (14.6)	10 (12.9)	0 (0)	0.419
Culprit lesion – RCA	321 (34.4)	383 (35.3)	247 (38.0)	137 (43.6)	33 (42.8)	5 (38.4)	0.051
PCI with drug-eluting stent	840 (90.2)	992 (91.6)	563 (86.6)	256 (81.5)	64 (83.1)	8 (61.5)	<0.001
CABG during hospitalisation	4 (0.4)	12 (1.1)	5 (0.7)	5 (1.5)	0 (0)	0 (0)	0.314
Mechanical support – IABP	87 (9.3)	117 (10.8)	106 (16.3)	64 (20.3)	10 (12.9)	4 (30.7)	<0.001
Mechanical support – PCPS	11 (1.1)	14 (1.2)	18 (2.7)	15 (4.7)	1 (1.2)	2 (15.3)	<0.001
In-hospital mortality	12 (1.2)	32 (2.9)	52 (8.0)	38 (12.1)	11 (14.2)	4 (30.7)	<0.001
Cardiovascular death, non-fatal MI, or non-fatal stroke	16 (1.7)	32 (2.9)	42 (6.4)	38 (12.1)	9 (11.6)	4 (30.7)	<0.001
Myocardial infarction	8 (0.8)	7 (0.6)	7 (1.0)	4 (1.2)	1 (1.2)	1 (7.6)	0.184
Stent thrombosis	4 (0.4)	6 (0.5)	4 (0.6)	0 (0)	1 (1.2)	0 (0)	0.480
BARC Type 3 or 5 bleeding	16 (1.7)	31 (2.8)	40 (6.1)	37 (11.7)	8 (10.3)	2 (15.3)	<0.001
Dual antiplatelet therapy	918 (98.6)	1,071 (98.9)	626 (96.3)	304 (96.8)	72 (93.5)	11 (84.6)	<0.001
ACEi/ARB	761 (81.7)	848 (78.3)	494 (76.0)	208 (66.2)	48 (62.3)	6 (46.1)	<0.001
Beta blocker	646 (69.3)	719 (66.4)	402 (61.8)	188 (59.8)	47 (61.0)	9 (69.2)	<0.001
Statin	884 (94.9)	1,015 (98.3)	563 (86.6)	254 (80.8)	63 (81.8)	12 (92.3)	<0.001

Values are presented as n (%). ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin II type 1 receptor blocker; BARC: Bleeding Academic Research Consortium; CABG: coronary artery bypass grafting; IABP: intra-aortic balloon pump; MI: myocardial infarction; PCI: percutaneous coronary intervention; PCPS: percutaneous cardiopulmonary support; RCA: right coronary artery

interventional characteristics of the patients. The overall in-hospital mortality rate was 4.9% (149/3,067), and a higher AHEAD score was associated with an increased in-hospital mortality rate ($p<0.001$).

Following univariate analyses, multivariable Cox regression was performed using the AHEAD score as the main variable, adjusting for male sex, hypertension, dyslipidaemia, peripheral artery disease, prior coronary artery bypass grafting, prior stroke, malignancy, STEMI, Killip classification (per class increase), door-to-device time <90 minutes, final TIMI flow, peak creatine kinase >1,672 IU/L (median), and left ventricular ejection fraction (**Table 3**). This analysis revealed that the AHEAD score was independently associated with an increased risk of all-cause mortality up to 1 year after acute MI (adjusted hazard ratio 1.60, 95% confidence interval: 1.39-1.84; $p<0.001$).

In a sensitivity analysis that included variables related to medical treatment (**Supplementary Table 1**), the AHEAD score remained independently associated with increased 1-year all-cause mortality. In Kaplan-Meier analysis, patients with higher AHEAD scores exhibited lower survival rates at 1 year following hospitalisation for acute MI (**Figure 1**).

The forest plot demonstrated that the AHEAD score was associated with all-cause mortality across all subgroups (**Figure 2**). Restricted cubic spline Cox regression demonstrated that an increasing AHEAD score was associated with a progressively higher risk of all-cause mortality (**Figure 3**).

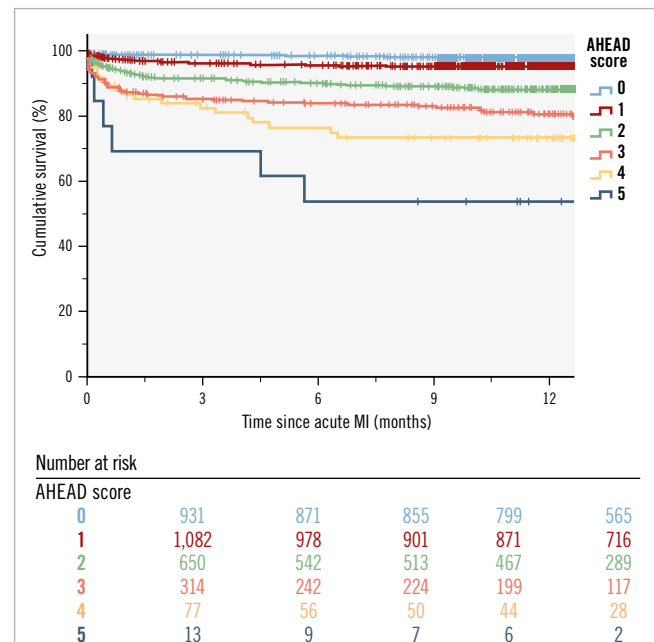


Figure 1. Kaplan-Meier analysis stratified by AHEAD score. Patients with higher AHEAD scores had a lower survival rate at 1 year following hospitalisation for acute myocardial infarction.

Table 3. Cox regression analysis for the prediction of 1-year mortality in patients with acute myocardial infarction.

	Univariate			Multivariate		
	HR	95% CI	p-value	aHR	95% CI	p-value
AHEAD score (per 1-point increase)	1.98	1.79-2.20	<0.001	1.60	1.39-1.84	<0.001
Variables						
Male	1.37	1.02-1.82	0.032	1.15	0.79-1.67	0.455
Hypertension	0.72	0.55-0.95	0.022	0.69	0.48-1.01	0.055
Dyslipidaemia	0.52	0.40-0.67	<0.001	0.43	0.31-0.60	<0.001
Peripheral artery disease	2.53	1.58-4.05	<0.001	1.73	1.00-3.02	0.050
Prior MI	1.28	0.84-1.94	0.243			
Prior coronary artery bypass grafting	1.91	1.01-3.60	0.045	1.18	0.54-2.60	0.655
Prior stroke	2.53	1.82-3.52	<0.001	1.22	0.79-1.89	0.360
Malignancy	2.64	1.88-3.69	<0.001	1.86	1.22-2.83	0.004
STEMI	0.55	0.48-1.00	0.055	0.57	0.35-0.93	0.026
Killip classification (per class increase)	2.28	2.07-2.52	<0.001	1.64	1.42-1.90	<0.001
Door-to-balloon time <90 min	0.52	0.40-0.68	<0.001	0.70	0.50-0.98	0.040
Final TIMI flow (per class increase)	0.67	0.55-0.82	<0.001	0.70	0.54-0.89	0.005
Peak creatine kinase concentration >1,672 IU/L	1.93	1.47-2.54	<0.001	1.33	0.93-1.89	0.112
Left ventricular ejection fraction, %	0.92	0.91-0.93	<0.001	0.95	0.93-0.96	<0.001

aHR: adjusted hazard ratio; CI: confidence interval; HR: hazard ratio; MI: myocardial infarction; STEMI: ST-segment elevation myocardial infarction; TIMI: Thrombolysis in Myocardial Infarction

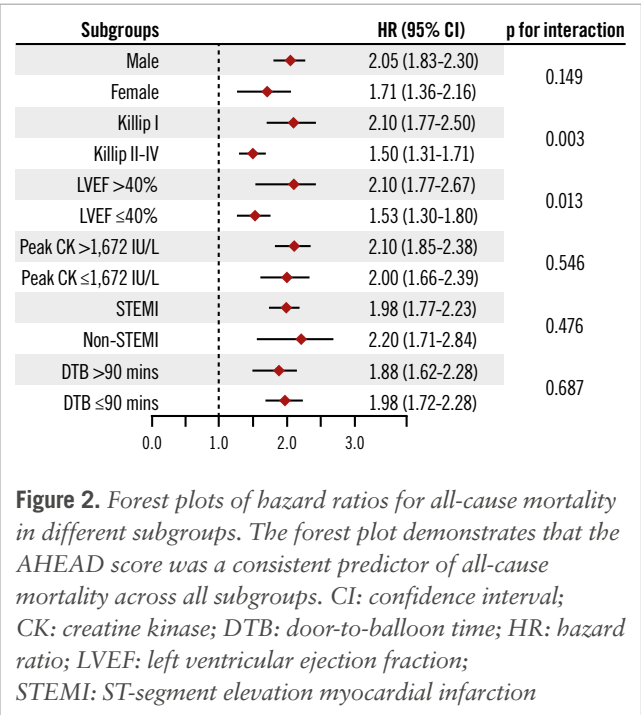


Figure 2. Forest plots of hazard ratios for all-cause mortality in different subgroups. The forest plot demonstrates that the AHEAD score was a consistent predictor of all-cause mortality across all subgroups. CI: confidence interval; CK: creatine kinase; DTB: door-to-balloon time; HR: hazard ratio; LVEF: left ventricular ejection fraction; STEMI: ST-segment elevation myocardial infarction

Discussion

In this multicentre study, we demonstrated that the AHEAD score, as a marker of HF, is predictive of all-cause mortality among patients with acute MI. Our results were consistent across multivariable Cox regression and stratified analyses in the forest plot (Central illustration).

According to their baseline characteristics, patients with a higher AHEAD score appeared to have more severe

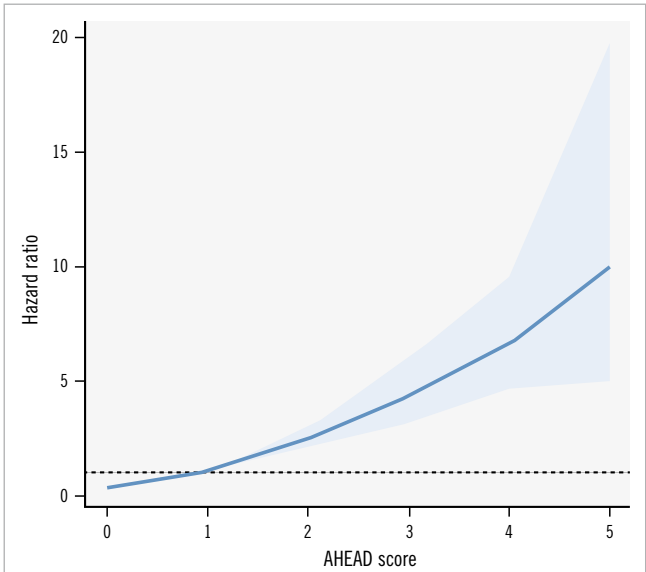


Figure 3. Restricted cubic spline Cox regression showing the association between the AHEAD score and all-cause mortality. An increasing AHEAD score was associated with a progressively higher risk of all-cause mortality. The median AHEAD score of 1 was used as the reference point (hazard ratio 1.0). The blue line represents the hazard ratio, and the shaded light blue area indicates the 95% confidence interval.

cardiovascular disease. In addition, late presentation – probably due to less prominent symptoms resulting from diabetic neuropathy – may have contributed to the

The AHEAD score as a useful marker of all-cause mortality in both acute MI and heart failure populations.

A

AHEAD score: Total ____ points (0-5)

Atrial fibrillation (1 pt)

Haemoglobin level (1 pt):

Hb <13 g/mL for male patients,
Hb <12 g/dL for female patients

Elderly (1pt): >70 years

Abnormal renal parameters (1 pt):

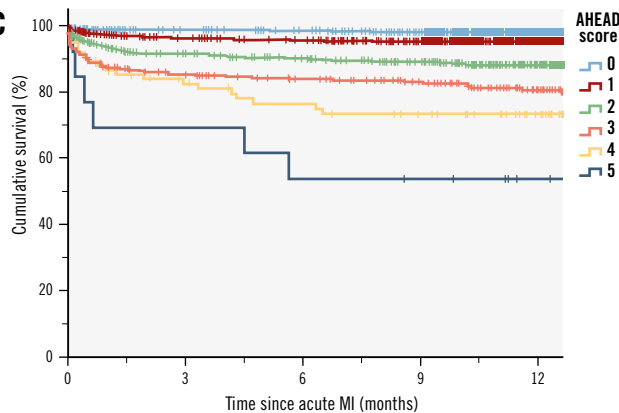
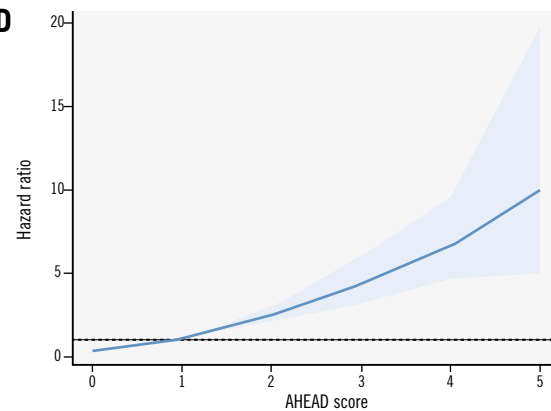
creatinine level >130 mol/L ($\approx$ 1.47 mg/dL)

Diabetes mellitus (1 pt)

In the Japanese Acute MI Registry (JAMIR),

AHEAD score $\uparrow$ all-cause mortality $\uparrow$ **B**

Subgroups	HR (95% CI)	p for interaction
Male	2.05 (1.83-2.30)	0.149
Female	1.71 (1.36-2.16)	
Killip I	2.10 (1.77-2.50)	0.003
Killip II-IV	1.50 (1.31-1.71)	
LVEF >40%	2.10 (1.77-2.67)	0.013
LVEF $\leq$ 40%	1.53 (1.30-1.80)	
Peak CK >1,672 IU/L	2.10 (1.85-2.38)	0.546
Peak CK $\leq$ 1,672 IU/L	2.00 (1.66-2.39)	
STEMI	1.98 (1.77-2.23)	0.476
Non-STEMI	2.20 (1.71-2.84)	
DTB >90 mins	1.88 (1.62-2.28)	0.687
DTB $\leq$ 90 mins	1.98 (1.72-2.28)	

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A) The AHEAD score points system; (B) all-cause mortality in different subgroups; (C) Kaplan-Meier analysis; (D) the association between the AHEAD score and all-cause mortality. CI: confidence interval; CK: creatine kinase; DTB: door-to-balloon time; HR: hazard ratio; LVEF: left ventricular ejection fraction; MI: myocardial infarction; STEMI: ST-segment elevation myocardial infarction

longer door-to-device times observed in patients with higher AHEAD scores, thereby complicating their systemic condition. Notably, patients with higher AHEAD scores were more likely to experience Bleeding Academic Research Consortium Type 3 or 5 bleeding during hospitalisation for acute MI, which may have led to a lower rate of PCI with drug-eluting stent use, as well as a reduced rate of dual antiplatelet therapy. In addition, they were less likely to receive angiotensin-converting enzyme inhibitors or angiotensin II type 1 receptor blockers, possibly due to unstable haemodynamics or lower blood pressure during the periprocedural period. This finding is consistent with the

fact that these patients had a higher incidence of Killip class III/IV and greater use of mechanical circulatory support during the same period.

Multivariate analysis demonstrated that the AHEAD score was independently associated with 1-year all-cause mortality following hospitalisation for acute MI. This result is comparable to that of a previous study in which patients with acute MI were excluded⁴. To the best of our knowledge, this is the first study in which the predictive value of the AHEAD score has been externally validated in a large cohort of Asian patients with acute MI, regardless of the presence or absence of acute HF. We demonstrated that the AHEAD

score can be used to accurately stratify the risk of all-cause mortality at 1 year in patients with acute MI, not only those with HF⁴. In subgroup analysis, the AHEAD score was found to be an independent predictor of all-cause mortality across all subgroups, suggesting that the AHEAD score is useful for predicting poor outcomes in acute MI, irrespective of the presence of HF.

Furthermore, we examined the association between the AHEAD score and all-cause mortality using a restricted cubic spline Cox model. The analysis demonstrated an overall upward trend, reflecting an increase in mortality risk with higher AHEAD scores. This association shown in the spline curve is consistent with the Kaplan-Meier curve, suggesting that the AHEAD score and risk of all-cause mortality have a linear relation. As described above, the AHEAD score, originally developed as a simple risk stratification tool for patients with acute HF, incorporates five components: atrial fibrillation, haemoglobin level, elderly age, abnormal renal function, and diabetes mellitus. Previous studies have demonstrated its utility in predicting mortality and hospitalisation in heart failure cohorts^{3,4}. In our analysis, the observed increase in hazard with higher AHEAD scores aligns with existing evidence showing that cumulative comorbidities adversely affect prognosis. However, the elevated risk observed among patients with lower AHEAD scores raises important questions. This subgroup may include individuals with unmeasured high-risk features such as frailty, active malignancy, or life-threatening bleeding events^{15,16}. Additionally, early mortality related to acute cardiovascular events may not be adequately captured by the components of the AHEAD score, which focus on chronic conditions. Such limitations emphasise that the AHEAD score, while useful, does not fully encompass the multidimensional nature of risk in contemporary patient populations. This finding supports the integration of complementary tools or biomarkers into risk assessment frameworks. Physicians should remain aware that risk prediction tools – while simple, accessible, and informative – require context-specific interpretation and should be augmented by clinical judgement and, where appropriate, additional risk markers.

Limitations

First, residual or unmeasured confounding factors may have remained in our analyses due to the observational nature of the study. Second, although the original study was conducted across 50 institutions throughout Japan, the selection process for participating hospitals may have introduced selection bias. In addition, limited ethnic diversity and interinstitutional variability in healthcare practices may restrict the generalisability of the findings. Third, only patients with acute MI who were treated with early revascularisation therapy – the vast majority of whom underwent PCI – were included; hence, our results may not be applicable to patients receiving alternative treatments. Finally, because the study was observational, the timing of blood sampling for creatine kinase measurement was not standardised in the study protocol and was instead determined by local hospital practices. As a result, peak creatine kinase concentrations may have been underestimated in certain cases.

Conclusions

The AHEAD score, a simple and validated marker of all-cause mortality in patients with acute HF, was also found to be associated with all-cause mortality in patients with acute MI at 1 year. This score may be useful because of its simplicity and clinical applicability, particularly in patients with acute MI complicated by HF.

Authors' affiliations

1. Department of Cardiology, Sakakibara Heart Institute, Tokyo, Japan; 2. Division of Cardiovascular Medicine, Department of Internal Medicine, Toho University Faculty of Medicine, Tokyo, Japan; 3. Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita, Japan; 4. Department of Cardiology, Miyazaki Medical Association Hospital, Miyazaki, Japan; 5. Department of Cardiology, Sakurajyuji Yatsushiro Rehabilitation Hospital, Kumamoto, Japan; 6. Department of Public Health and Health Policy, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Japan; 7. Department of Preventive Medicine and Epidemiology, National Cerebral and Cardiovascular Center, Suita, Japan; 8. Department of Cardiology, Tokyo Medical University Hospital, Tokyo, Japan; 9. Department of Cardiology, Yokohama City University Graduate School of Medicine, Yokohama, Japan; 10. Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan; 11. Kumamoto University, Kumamoto, Japan; 12. Division of Cardiology, Yokohama City University Medical Center, Yokohama, Japan

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Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nwacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2022;79:e263-421.
2. Sakata Y, Shimokawa H. Epidemiology of heart failure in Asia. *Circ J*. 2013;77:2209-17.
3. Spinar J, Jarkovsky J, Spinarova L, Mebazaa A, Gayat E, Vitovec J, Linhart A, Widimsky P, Miklik R, Zeman K, Belohlavek J, Malek F, Felsoci M, Kettner J, Ostadal P, Cihalik C, Vaclavik J, Taborsky M, Dusek L, Littnerova S, Parenica J. AHEAD score—Long-term risk classification in acute heart failure. *Int J Cardiol*. 2016;202:21-6.

4. Chen YJ, Sung SH, Cheng HM, Huang WM, Wu CL, Huang CJ, Hsu PF, Yeh JS, Guo CY, Yu WC, Chen CH. Performance of AHEAD Score in an Asian Cohort of Acute Heart Failure With Either Preserved or Reduced Left Ventricular Systolic Function. *J Am Heart Assoc.* 2017;6:e004297.
5. Miyachi H, Yamamoto T, Takayama M, Miyauchi K, Yamasaki M, Tanaka H, Yamashita J, Kishi M, Higuchi S, Abe K, Mase T, Shinke T, Yahagi K, Wakabayashi K, Asano T, Minatsuki S, Saji M, Iwata H, Mitsuhashi Y, Ito R, Kondo S, Shimizu W, Nagao K. 10-Year Temporal Trends of In-Hospital Mortality and Emergency Percutaneous Coronary Intervention for Acute Myocardial Infarction. *JACC Asia.* 2022;2:677-88.
6. Takii T, Yasuda S, Takahashi J, Ito K, Shiba N, Shirato K, Shimokawa H; MIYAGI-AMI Study Investigators. Trends in acute myocardial infarction incidence and mortality over 30 years in Japan: report from the MIYAGI-AMI Registry Study. *Circ J.* 2010;74:93-100.
7. Ozaki Y, Katagiri Y, Onuma Y, Amano T, Muramatsu T, Kozuma K, Otsuji S, Ueno T, Shiode N, Kawai K, Tanaka N, Ueda K, Akasaka T, Hanaoka KI, Uemura S, Oda H, Katahira Y, Kadota K, Kyo E, Sato K, Sato T, Shite J, Nakao K, Nishino M, Hikichi Y, Honye J, Matsubara T, Mizuno S, Muramatsu T, Inohara T, Kohsaka S, Michishita I, Yokoi H, Serruys PW, Ikari Y, Nakamura M; Task Force on Primary Percutaneous Coronary Intervention (PCI) of the Japanese Cardiovascular Interventional Therapeutics (CVIT). CVIT expert consensus document on primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) in 2018. *Cardiovasc Interv Ther.* 2018;33:178-203.
8. Saito Y, Kobayashi Y. Contemporary coronary drug-eluting and coated stents: a mini-review. *Cardiovasc Interv Ther.* 2021;36:20-2.
9. Yasuda S, Honda S, Takegami M, Nishihira K, Kojima S, Asaumi Y, Suzuki M, Kosuge M, Takahashi J, Sakata Y, Takayama M, Sumiyoshi T, Ogawa H, Kimura K; JAMIR Investigators. Contemporary Antiplatelet Therapy and Clinical Outcomes of Japanese Patients With Acute Myocardial Infarction - Results From the Prospective Japan Acute Myocardial Infarction Registry (JAMIR). *Circ J.* 2019;83:1633-43.
10. Saito Y, Kobayashi Y, Tanabe K, Ikari Y. Antithrombotic therapy after percutaneous coronary intervention from the Japanese perspective. *Cardiovasc Interv Ther.* 2020;35:19-29.
11. Nishihira K, Honda S, Takegami M, Kojima S, Asaumi Y, Suzuki M, Kosuge M, Takahashi J, Sakata Y, Takayama M, Sumiyoshi T, Ogawa H, Kimura K, Yasuda S; JAMIR investigators. Impact of bleeding on mortality in patients with acute myocardial infarction complicated by cardiogenic shock. *Eur Heart J Acute Cardiovasc Care.* 2021;10:388-96.
12. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Writing Group on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. *Glob Heart.* 2012;7:275-95.
13. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation.* 1994;90:583-612.
14. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger CB, Steg PG, Gore JM, Budaj A, Avezum A, Flather MD, Fox KA; GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. *JAMA.* 2004;291:2727-33.
15. Völschow B, Gofßling A, Kellner C, Neumann JT. Frailty prevalence, invasive treatment frequency, and in-hospital outcome in patients hospitalized for acute coronary syndrome in Germany (2005-2022): a nationwide registry study. *Lancet Reg Health Eur.* 2024;49:101168.
16. Pedersen F, Butrymovich V, Kelbæk H, Wachtell K, Helqvist S, Kastrup J, Holmvang L, Clemmensen P, Engstrøm T, Grande P, Saunamäki K, Jørgensen E. Short- and long-term cause of death in patients treated with primary PCI for STEMI. *J Am Coll Cardiol.* 2014;64:2101-8.

Supplementary data

Supplementary Table 1. Cox regression analysis for the prediction of 1-year mortality in patients with acute myocardial infarction.

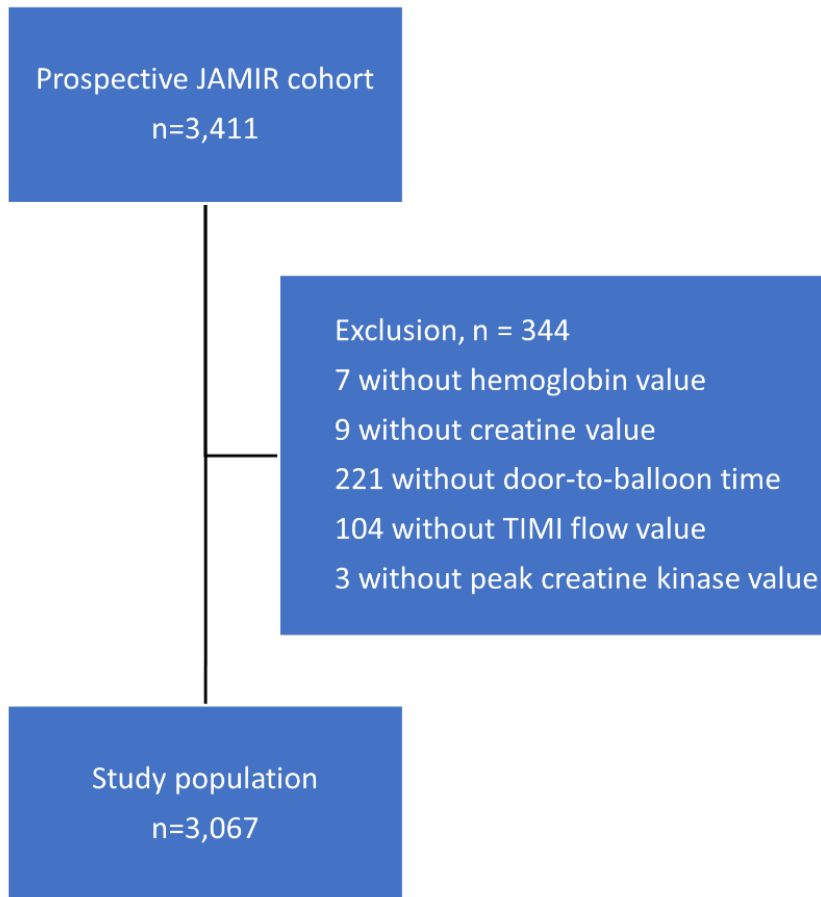
Supplementary Figure 1. Flowchart of the study population.

Data availability statement

Ethics statement

The supplementary data are published online at:
<https://AsiaIntervention.pcronline.com/doi/10.4244/AIJ-D-25-00020>





Supplementary Figure 1. Flowchart of the study population.

A flowchart illustrating the total number of patients included and excluded.

JAMIR: Japan Acute Myocardial Infarction Registry; TIMI: Thrombolysis In Myocardial Infarction.

Data availability

The de-identified participant data will be shared on a request basis. Please directly contact the corresponding author to request data sharing.

Ethics statement

The JAMIR research protocol was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center and by the local ethics committees or local institutional review boards at each study site (M27-019-12).