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ORIGINAL RESEARCH

Prediction of In-Hospital Mortality for Ischemic Cardiogenic Shock Requiring Venoarterial Extracorporeal Membrane Oxygenation

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BACKGROUND: Clinical outcome of ischemic cardiogenic shock (CS) requiring extracorporeal membrane oxygenation is highly variable, necessitating appropriate assessment of prognosis. However, a systemic predictive model estimating the mortality of refractory ischemic CS is lacking. The PRECISE (Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support) score was developed to predict the prognosis of refractory ischemic CS due to acute myocardial infarction.

METHODS AND RESULTS: Data were obtained from the multicenter CS registry RESCUE (Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Assist Device for Korean Patients With Cardiogenic Shock) that consists of 322 patients with acute myocardial infarction complicated by refractory ischemic CS requiring extracorporeal membrane oxygenation support. Fifteen parameters were selected to assess in-hospital mortality. The developed model was validated internally and externally using an independent external cohort (n=138). Among 322 patients, 138 (42.9%) survived postdischarge. Fifteen predictors were included for model development: age, diastolic blood pressure, hypertension, chronic kidney disease, peak lactic acid, serum creatinine, lowest left ventricular ejection fraction, vasoactive inotropic score, shock to extracorporeal membrane oxygenation insertion time, extracorporeal cardiopulmonary resuscitation, use of intra-aortic balloon pump, continuous renal replacement therapy, mechanical ventilator, successful coronary revascularization, and staged percutaneous coronary intervention. The PRECISE score yielded a high area under the receiver-operating characteristic curve (0.894 [95% CI, 0.860–0.927]). External validation and calibration resulted in competent sensitivity (area under the receiver-operating characteristic curve, 0.895 [95% CI, 0.853–0.930]).

CONCLUSIONS: The PRECISE score demonstrated high predictive performance and directly translates into the expected in-hospital mortality rate. The PRECISE score may be used to support clinical decision-making in ischemic CS (www.theprecisescore.com).

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02985008.

Key Words: extracorporeal membrane oxygenation ■ hospital mortality ■ myocardial ischemia ■ shock, cardiogenic

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CLINICAL PERSPECTIVE

What Is New?

- The PRECISE (Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support) score includes 15 clinical parameters that reflect severity of shock and its therapeutic outcome to assess in-hospital mortality after ischemic cardiogenic shock.
- Data were derived from the homogenous population of refractory ischemic cardiogenic shock after acute myocardial infarction who received extracorporeal membrane oxygenation.

What Are the Clinical Implications?

- The PRECISE score is directly translated as an expected in-hospital mortality rate, that can be used for patients with acute myocardial infarction and refractory ischemic cardiogenic shock requiring extracorporeal membrane oxygenation.
- The PRECISE score provides prognostic information in a critical phase of shock that enables optimal further decision-making.

Nonstandard Abbreviations and Acronyms

AIC	Akaike's information criterion
CRRT	continuous renal replacement therapy
CS	cardiogenic shock
ECPR	extracorporeal cardiopulmonary resuscitation
IABP	intra-aortic balloon pump

Cardiogenic shock (CS) is a critical consequence of acute myocardial injury, primarily due to acute myocardial infarction (AMI), cardiomyopathy, myocarditis, etc.[1] Despite the consistent development of therapeutic interventions and advances in mechanical circulatory support, the mortality of CS remains high.[2–4] Ischemic CS accounts for up to 80%, and results in worse prognosis compared with nonischemic CS.[5] Even after prompt revascularization, prognosis of ischemic CS varies widely, depending on the optimal revascularization of the culprit lesion, which is difficult to predict in clinical practice.

Short-term mechanical circulatory support including venoarterial extracorporeal membrane oxygenation (ECMO) is widely used until the recovery from hypoperfusion. However, use of ECMO does not always guarantee favorable outcome. In a recent randomized trial, early and routine deployment of venoarterial ECMO in CS after AMI revealed no mortality benefit compared with medical therapy alone.[6] That is, deterioration of shock refractory to ECMO leads to death, and other complications (ie, brain injury, ECMO-related bleeding, or infection) also contribute to mortality. Therefore, assessing the prognosis of refractory ischemic CS is critical for further decision-making and clinical use of limited medical resources, even after initiation of mechanical circulatory support. Several studies have assessed the prognosis of patients with CS requiring venoarterial ECMO.[3,7–11] However, several limitations lie in using previous prediction scores on patients with refractory ischemic CS. Previous prediction scores have either involved a heterogenous population of CS with various origin or had a small sample and lack of external validation. In this regard, we developed the PRECISE (Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support) score to assess the prognosis of refractory ischemic CS patients with ECMO insertion using a multicenter, dedicated CS registry database.

METHODS

Study Population

The developmental cohort of the PRECISE score was derived from the RESCUE registry (Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Assist Device for Korean Patients With Cardiogenic Shock, NCT02985008 at www.clinicaltrials.gov), which is a multicenter, retrospective and prospective cohort of consecutive patients admitted with CS. Patients were enrolled from 12 tertiary centers across all geographical regions of Korea, which includes 1247 patients from January 2014 to December 2018. The validation cohort was developed using external data from a single-center (Samsung Medical Center, Seoul, Korea) venoarterial ECMO cohort (n=213) between January 2010 and August 2021. Samsung Medical Center is a highly experienced intensive care unit capable of venoarterial ECMO management, as well as receiving patients requiring ECMO insertion from other hospitals. There was no overlap of data between external (n=213) and developmental data (n=1247).

Written informed consent was obtained from all participants or their legal representatives. This study was approved by the institutional review board of each hospital (IRB No. 2016-03-130). The study complied with the principles of the Declaration of Helsinki. All data generated or analyzed during this study are included in this published article and its supplementary information files.

Data Collection and Management of Cardiogenic Shock

Detailed protocol and further information about data collection for the RESCUE registry were published previously.[12] Adult patients >19-years old were enrolled under the following inclusion criteria: (1) systolic blood pressure <90 mm Hg despite volume resuscitation or in need of inotropes; and (2) sign of end organ hypoperfusion defined as cool extremity, oliguria (<0.5 mL/Kg per hour), altered mentality, lactate ≥2.0 mmol/L, or sign of pulmonary edema. Patients were excluded if (1) shock occurred after out-of-hospital cardiac arrest, (2) there was evidence of shock of origin other than cardiogenic (hypovolemic, septic, or neurogenic) shock, or (3) they requested to discontinue participation in the study. Patients were further classified according to the cause of shock: ischemic or nonischemic CS. Ischemic CS was defined as clinical and angiographic evidence of myocardial ischemia that predisposes to CS, which includes ST-elevation myocardial infarction (MI), non-ST-elevation MI, unstable angina, stable angina, variant angina, or ischemic cardiomyopathy.[13,14] Among ischemic CS, AMI was defined as either ST-elevation MI or non-ST-elevation MI.

The inotropic score and vasoactive-inotropic score were calculated with the maximal requirement of vasoactive agents during the first 48 hours of shock, including norepinephrine, milrinone, vasopressin, dopamine, dobutamine, epinephrine, using the following formula as described by Gaies et al.[15] Adequate interventions such as coronary angiography, percutaneous coronary intervention (PCI), mechanical circulatory support, ECMO or intra-aortic balloon pump (IABP) insertion, continuous renal replacement therapy (CRRT), and intubation with mechanical ventilator proceeded promptly based on the patient's indication. 2D-echocardiography was examined at the presentation of shock and followed up upon clinical need. Left ventricular ejection fraction (LVEF) was measured by modified Simpson's method, and only formal echocardiographic records were obtained.

Statistical Analysis

The PRECISE score for predicting in-hospital mortality was developed according to published recommendations[16,17] using a multivariable logistic regression model with a derivation cohort of 322 patient data sets. The steps for the score development are as follows:

Step 1: Identification of "Candidate Predictors"

For the data set of 322 patients, 67 variables related to patients' demographic, clinical, and biological characteristics were initially considered (Table S1). The variables were summarized as numbers and percentages for categorical variables and as means and SDs for continuous variables. Comparisons between survivors and nonsurvivors were performed using the chi-square test or Fisher's exact test for categorical variables and the Student's *t* test for continuous variables. Potential outliers and missing patterns of variables were examined, and variables with <5% missing values were considered potential candidate variables for the prediction model. Two variables (lowest LVEF, peak lactic acid) revealed higher missing values but were included for analysis regarding their clinical significance (Figure S1). Continuous variables with missing values were imputed using their medians, whereas categorical variables were imputed randomly according to the observed percentages of nonmissing data. After examining multicollinearity among the explanatory variables, residual diagnostics of the multiple logistic regression models were performed. Candidate predictors were then selected by using the –2 log-likelihood test result (*P* value <0.05), which were –2 times the difference of log-likelihood statistic from the univariable logistic regression model (ie, including one variable in a model at a time) to the null model (ie, a model with intercept only), as well as with a negative change in the Akaike's information criterion (AIC) statistic. Penalized regression approaches (least absolute shrinkage selector operator regression and elastic net regression) were additionally performed to compare candidate predictors (Table S2). Further definition of selected predictors is provided in Table S3.

Step 2: Model Development

To find an appropriate transformation of continuous variables for predicting in-hospital mortality, the fit of a simple logistic regression model with linear, inverse, logarithmic, square root, square, or cubic transformations of the variables was examined. The AIC statistics of the fitted model were compared with those of the linear transformation model. An appropriate transformation type for each continuous variable was chosen if the change in the AIC was noticeable compared with that of the linear transformation.

The selected parameters were subsequently used to examine significant interactions between the predictors. A full second-order multiple logistic regression model with all possible 2-way interaction terms among predictors was built, and significant interactions (*P* value <0.05) between the variables were chosen to construct the final prediction model for in-hospital mortality.

Step 3: Internal Validation

Internal validation was performed using a multivariable logistic regression model to assess the performance

of the prediction model on the original data set. Regression parameter estimates were reestimated using 1000 bootstrap samples.[18] Harrel's C-statistic for model performance, the mean Brier score for discrimination ability, a discrimination slope for agreement between predicted and observed probabilities, and Nagelkerke's R^2 for variation explained were used for internal validation.[16]

Step 4: External Validation

To calibrate and revise the regression coefficients of the developed model, external validation was performed using prospectively enrolled patients with ECMO-inserted refractory ischemic CS in a single-center venoarterial ECMO registry data set. To revise the regression parameter estimates, the overall intercept and slopes of the parameters were calibrated by re-fitting a null model, using the linear predictors of the developed model as an offset variable.[16] The area under the receiver operating characteristic curve (AUC), mean Brier score, discrimination slope, and Nagelkerke's R^2 were used to validate the performance of the final prediction score. Chi-square goodness-of-fit test was performed to assess the model fitness of the final prediction model.

All statistical analyses and model development were performed using the SAS software (version 9.4; SAS Inc., Cary, NC, USA).

RESULTS

Study Population

A total of 1247 patients with CS were enrolled from 12 tertiary centers in Korea between January 2014 and December 2018 (Figure 1). Among them, 496 underwent venoarterial ECMO insertion, and 360 were classified as having ischemic CS. 322 were diagnosed with AMI of either ST-elevation myocardial infarction (MI) and non-ST-elevation MI, and were included for development of the PRECISE score.

Baseline Characteristics and Demographics

Table 1 shows the baseline characteristics of patients who underwent refractory ischemic CS with ECMO insertion. Among the 322 patients with refractory ischemic CS who received ECMO, 138 (42.9%) were alive at hospital discharge. The mean age was 65.2±12.1 years, with patients predominantly being

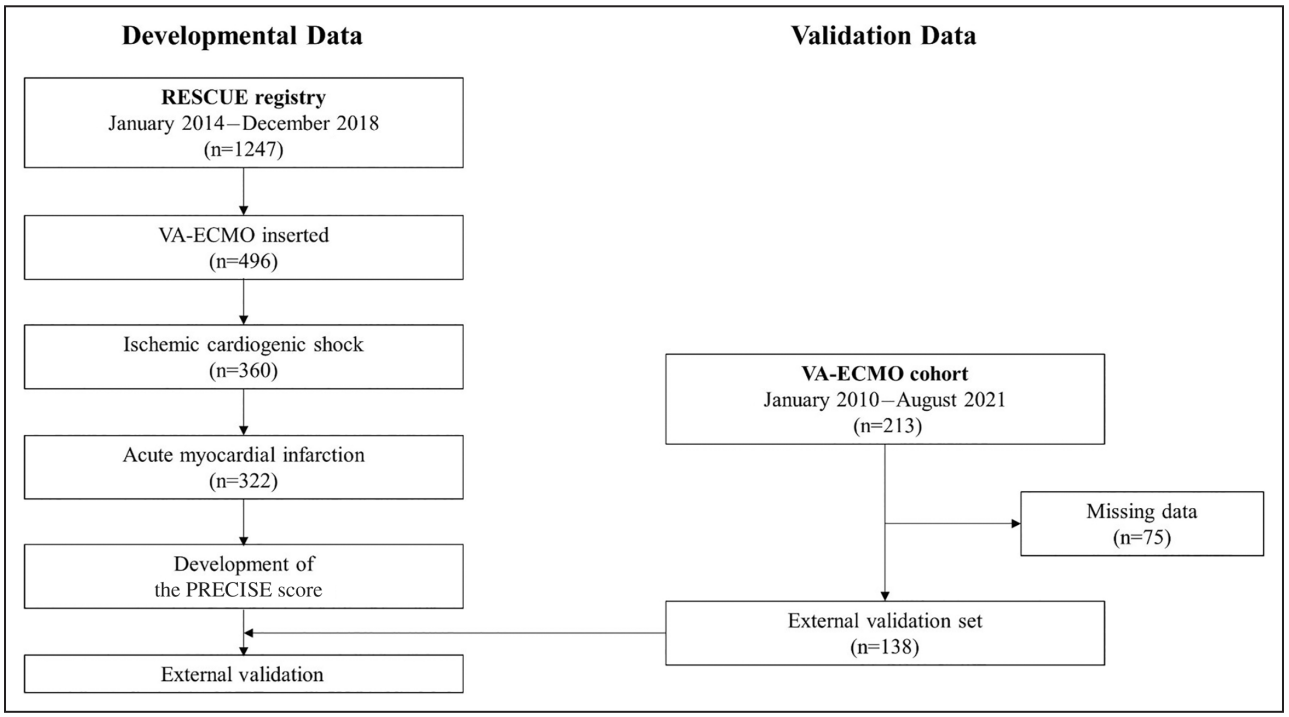


Figure 1. Clinical flow chart.
Clinical flow chart of enrollment of RESCUE registry. PRECISE indicates Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support; RESCUE, Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Assist Device for Korean Patients With Cardiogenic Shock; and VA-ECMO, venoarterial extracorporeal membrane oxygenation.

men (74.8%). Coronary angiography was performed in 308 (95.7%) patients and 295 (91.6%) were successfully revascularized using either PCI or a coronary artery bypass graft.

Compared with nonsurvivors, survivors were younger and presented with a higher initial systolic blood pressure and diastolic blood pressure. Survivors also revealed lower inotropic score and vasoactive inotropic score. The proportion of extracorporeal cardiopulmonary resuscitation (ECPR) was significantly lower, and adjunctive therapy was less frequently used in survivors including IABP, CRRT, and mechanical ventilation. Survivors had shorter duration of shock before ECMO insertion, and higher LVEF. Among the laboratory markers, only creatinine and lactic acid levels differed between survivors and nonsurvivors. Other ECMO-related variables and complications are described in Table S4. Although no significant differences were found between the 2 groups in terms of ECMO-related complications (limb ischemia, ECMO site bleeding, stroke, gastrointestinal bleeding, sepsis), nonsurvivors showed higher tendency of ECMO site bleeding, gastrointestinal bleeding, and sepsis.

Predictors for In-Hospital Death and Model Development

No potential extreme observations were found in the data set of 322 patients with 67 demographic and clinical variables. Collinearities between systolic and diastolic blood pressure were suspected (variance inflation factor, 6.54 and 6.59, respectively); hence, systolic blood pressure was excluded from the prediction model. For variable selection, logistic regression approach was selected. Residual diagnostics using a multiple logistic regression model revealed neither outliers nor influential observations. After examining the –2 log-likelihood test result and the AIC statistic between univariable and null models, 15 candidate predictors for in-hospital mortality were chosen: age, diastolic blood pressure, hypertension, chronic kidney disease, ECPR, successful coronary revascularization, staged PCI, use of IABP or CRRT or a mechanical ventilator, shock to ECMO insertion time (min), lowest LVEF (%), serum creatinine (mg/dL), peak lactic acid (mmol/L), and vasoactive inotropic score (Table 2).

After examining the appropriate transformation for 7 continuous variables, no transformation was used. Significant interactions were found between the following variables: age and peak lactic acid level, age and ECPR, age and use of CRRT, lowest LVEF and ECPR, serum creatinine and chronic kidney disease, serum creatinine and use of CRRT, peak lactic acid and hypertension, peak lactic acid and successful coronary revascularization, successful coronary revascularization and use of CRRT, and use of IABP and ECPR. The final model consisted of 15 predictors, including 7 numeric variables and 8 binary variables.

Model Validation and the PRECISE Score

The prediction model with a developmental data set of 322 patients with refractory ischemic CS showed an AUC of 0.894 (95% confidence interval, 0.860–0.927), mean Brier score of 0.129, a discrimination slope of 0.477, and the Nagelkerke's R^2 of 41.2% (Figure 2, Table S5).

After the PRECISE score was developed and internally validated to predict in-hospital mortality, it was calibrated using an external cohort of patients on venoarterial ECMO. Among the 213 patients in the external cohort, 138 were used for external validation of the prediction model as they had complete data for all the required variables. The model was externally validated by calibrating the model parameters of the intercepts and slopes. Table S6 compares the predictors used in the prediction model between the developmental data and those used for the external validation. Plots comparing the observed and model-predicted probabilities before and after calibration are shown in Figure S2.

The final PRECISE score for predicting in-hospital mortality is shown in Figure 3A.

Predicted probability of in-hospital death=exp (linear predictor)/[1+exp (linear predictor)], in where linear predictor=13.3759–0.0076×(age)–0.0057×(diastolic blood pressure)–0.0695×(lowest LVEF)+0.7519×(serum creatinine)+0.2416×(Peak lactic acid)–0.00134×(vasoactive inotropic score)+0.00015×(Shock to ECMO time)–1.2763×(hypertension)+0.3564×(chronic kidney disease)–14.2562×(successful coronary revascularization)+1.2956×(staged PCI)+0.6769×(use of IABP)+0.1661×(ECPR)–18.9556×(use of CRRT)–0.7773×(use of mechanical ventilator)+0.0061×(age)×(peak lactic acid)–0.0498×(age)×(ECPR)+0.0498×(age)×(use of CRRT)+0.0842×(lowest LVEF)×(ECPR)–0.4271×(serum creatinine)×(chronic kidney disease)–0.4242×(serum creatinine)×(use of CRRT)+0.2164×(peak lactic acid)×(hypertension)–0.6107×(peak lactic acid)×(successful coronary revascularization)+17.8809×(successful coronary revascularization)×(use of CRRT)–2.9114×(use of IABP)×(ECPR). (Online calculator available at www.theprecisescore.com).

External validation demonstrated adequate model performance: the intercept- and slope-calibrated model yielded an AUC of 0.895 (95% CI, 0.853–0.930), a mean Brier score of 0.112, a discrimination slope of 0.373, and the Nagelkerke's R^2 of 48.7%. (Figure 3B). Chi-square goodness-of-fit test revealed no significant difference of the observed outcome and the outcome predicted by the PRECISE score (Table S7).

Table 1. Baseline Characteristics of Patients With Refractory Ischemic CS With ECMO Insertion

Variables	Total (n=322)	Survivor (n=138)	Nonsurvivor (n=184)	*P* value
Age, y	65.2±12.1	62.6±11.3	67.3±12.3	0.001
Male sex	241 (74.8)	105 (76.1)	136 (73.9)	0.658
Body mass index, kg/m^2	23.5±3.2	23.5±3.5	23.5±3.0	0.930
Medical history				
Hypertension	173 (53.7)	64 (46.4)	109 (59.2)	0.022
Diabetes	137 (42.5)	60 (43.5)	77 (41.8)	0.770
Dyslipidemia	80 (24.8)	29 (21.0)	51 (27.7)	0.164
Chronic kidney disease	26 (8.1)	5 (3.6)	21 (11.4)	0.011
Previous myocardial infarction	48 (14.9)	19 (13.8)	29 (15.8)	0.621
Previous peripheral arterial occlusive disease	10 (3.1)	4 (2.9)	6 (3.3)	0.853
Previous PCI	57 (17.7)	23 (16.7)	34 (18.5)	0.675
Previous coronary artery bypass graft	11 (3.4)	5 (3.6)	6 (3.3)	0.860
Previous cerebrovascular accident	27 (8.4)	12 (8.7)	15 (8.2)	0.862
Previous CPR	13 (4.0)	10 (7.2)	3 (1.6)	0.021
Malignancy	18 (5.6)	7 (5.1)	11 (6.0)	0.727
Current smoking	104 (32.3)	48 (34.8)	56 (30.4)	0.411
Clinical presentation				
Systolic blood pressure, mm Hg	64.8±33.2	69.2±31.5	61.5±34.1	0.036
Diastolic blood pressure, mm Hg	42.8±23.0	47.5±22.2	39.3±23.1	0.002
Heart rate, beats/min	78.3±38.6	82.8±36.5	75.0±39.9	0.074
Use of norepinephrine	230 (71.4)	88 (63.8)	142 (77.2)	0.010
Use of epinephrine	43 (13.4)	11 (8.0)	32 (17.4)	0.010
Use of dobutamine	161 (50.0)	67 (48.6)	94 (51.1)	0.654
Use of dopamine	215 (66.8)	83 (60.1)	132 (71.7)	0.031
Use of vasopressin	38 (11.8)	11 (8.0)	27 (14.7)	0.056
Use of milrinone	15 (4.7)	6 (4.3)	9 (4.9)	0.820
Inotropic score*	28.5±43.2	20.5±27.7	34.4±51.1	0.002
Vasoactive inotropic score*	107.1±131.2	69.8±98.4	135.0±145.3	<0.001
Extracorporeal CPR	179 (55.6)	59 (42.8)	120 (65.2)	<0.001
Ischemic cardiomyopathy	287 (89.1)	114 (82.6)	173 (94.0)	0.002
ST-elevation myocardial infarction	193 (59.9)	84 (60.9)	109 (59.2)	0.769
Shock to ECMO insertion time, min	329.6±744.0	214.1±564.0	416.3±845.7	0.011
Use of intra-aortic balloon pump	51 (15.8)	15 (10.9)	36 (19.6)	0.034
Use of continuous renal replacement therapy	122 (37.9)	27 (19.6)	95 (51.6)	<0.001
Use of mechanical ventilator	273 (84.8)	100 (72.5)	173 (94.0)	<0.001
Lowest left ventricular ejection fraction (%)	26.8±12.8	29.9±14.0	24.5±11.3	0.000
Coronary angiography done†	308 (95.7)	132 (95.7)	176 (95.7)	1.000
Successful revascularization†	295 (91.6)	134 (97.1)	161 (87.5)	0.002
Staged PCI†	16 (5.0)	12 (8.7)	4 (2.3)	0.008
Culprit-only revascularization†	186 (60.4)	80 (60.6)	106 (60.2)	0.947
Multivessel revascularization†	86 (27.9)	38 (28.8)	48 (27.3)	0.770
Laboratory markers				
Hemoglobin, g/dL	12.6±2.7	12.8±2.5	12.5±2.8	0.287
Platelet count (×10^3/μL)	208.4±85.1	216.1±86.8	202.6±83.6	0.164
Creatinine, mg/dL	1.6±1.3	1.4±1.1	1.7±1.5	0.021

(*Continued*)

Table 1. Continued

Variables	Total (n=322)	Survivor (n=138)	Nonsurvivor (n=184)	*P* value
Peak lactic acid, mmol/L	8.5±4.6	7.1±4.2	9.5±4.6	<0.001
Peak troponin-I, ng/mL	87.9±523.9	97.1±156.6	81.1±176.1	0.409
Peak creatine kinase-MB, ng/mL	275.3±523.9	219.6±209.6	317.8±668.6	0.098
N-terminal pro-B-type natriuretic peptide, pg/mL	7896.1±12872.9	7863.8±15199.4	7924.3±10518.9	0.975
Duration of ECMO, d	5.0±4.7	4.9±5.0	5.3±4.2	0.573
Duration of intensive-care-unit stay, d	12.0±14.9	17.6±17.3	7.8±11.2	<0.001
Duration of admission, d	19.6±26.2	34.0±32.5	8.9±12.5	<0.001

Data are presented as frequencies (percentages) or as means±SD. CPR indicates cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; and PCI, percutaneous coronary intervention.

*Inotropic score=dopamine dose (μg/Kg per minute)+dobutamine dose (μg/Kg per minute)+100×epinephrine dose (μg/Kg per minute), and vasoactive-inotropic score=dopamine dose (μg/Kg per minute)+dobutamine dose (μg/Kg per minute)+100×epinephrine dose (μg/Kg per minute)+10×milrinone dose (μg/Kg per minute)+10000×vasopressin dose (units/Kg per minute)+100×norepinephrine dose (μg/Kg per minute).

†Result of coronary revascularization (successful revascularization and complete revascularization) was assessed in patients who underwent coronary angiography (n=308).

DISCUSSION

In this study, we developed a novel prediction model comprising clinical parameters in patients with refractory ischemic CS requiring ECMO. The major findings of this study are as follows. First, the PRECISE score is one of the first systematic prediction models for ECMO patients that focuses on a homogenous group of ischemic CS (Figure 4). It is based on data from a multicenter registry in Korea that includes the largest number of patients with refractory ischemic CS. Second, the PRECISE score is calculated directly from parameters that can be acquired in the during critical phase of CS after ECMO insertion. Third, clinically important and easily measured variables were included as predictors to reflect the severity of refractory ischemic CS in the real world. Several clinical indicators of hypoperfusion were included in the equation, which enhance predictive power. Finally, the PRECISE score was successfully validated and refined using external data, with its prognostic value outweighing previous prediction scores.[7–9,19]

Clinical Significance of the Prediction Model in Refractory Ischemic CS

Over the past 2 decades, remarkable advancements have been made in the therapeutic strategies for ischemic CS, especially in mechanical circulatory support devices. ECMO is the mainstay for cardiopulmonary support in patients with ischemic CS after revascularization and has been increasingly used in patients with CS.[20–22] Despite the efforts to improve survival outcomes for refractory CS, in-hospital survival rate remains suboptimal, barely exceeding 40%.[21] In this study, focusing on patients with AMI and refractory ischemic CS needing ECMO insertion, in-hospital mortality rate exceeded 50%. Patients experiencing ventricular failure after AMI undergo a dynamic clinical course, ranging from a stunned myocardium to irreversible myocardial necrosis, which may be reversed by expeditious coronary revascularization. Its distinctive characteristics emphasize the necessity for precise prediction of prognosis at the initial presentation of shock, which substantially influences proper clinical decisions. Moreover, precise assessment of in-hospital mortality in refractory ischemic CS is important for the proper distribution of limited medical resources, optimal decision-making, and providing information to patients' legal representatives.

Previous Prediction Scores

Several prediction models have been introduced for risk stratification of CS with venoarterial ECMO support, further focusing on ischemic origin.[7–9] A large-scale study presented a mortality prediction model using 3846 patients with CS who received ECMO insertion (the survival after venoarterial-ECMO score).[7] It is the first prediction model for in hospital survival in patients with refractory CS of ECMO use. However, the heterogeneous study cohort, including patients with CS of various causes, limited the assessment of the prognosis of ischemic CS. Muller et al. presented the Prediction of Cardiogenic Shock Outcome for AMI Salvaged by Veno-arterial ECMO score that estimates the prognosis of patients with AMI who received venoarterial ECMO (AUC, 0.84).[8] The score was derived from a relatively small number of patients (n=138) from only 2 intensive care units and without external validation. Nonetheless, the Prediction of Cardiogenic Shock Outcome for AMI Salvaged by Veno-arterial ECMO score is advantageous in that it could be used in the early phase of CS, as it covers only pre-ECMO insertion parameters. Recently, Ceglarek et al. proposed the cystatin C, lactate, interleukin-6, and N-terminal

Table 2. Model Development: Akaike's Information Criterion of the Fitted Model

	Simple model		Reduced model	
	Δ AIC	*P* value	Δ AIC	*P* value
Age	−9.923	0.0007	−15.099	<0.0001
Diastolic blood pressure	−8.275	0.0020	−2.669	0.0380
Hypertension	−3.254	0.0224	−0.637	0.1068
Chronic kidney disease	−5.039	0.0160	1.997	0.9595
Peak lactic acid	−20.828	<0.0001	−8.567	0.0018
Serum creatinine	−3.724	0.0387	1.908	0.7589
Lowest left ventricular ejection fraction	−12.050	0.0003	−11.850	0.0004
Vasoactive inotropic score	−19.901	<0.0001	−2.999	0.0318
Shock to extracorporeal membrane oxygenation insertion time	−4.565	0.0232	1.673	0.5732
Extracorporeal cardiopulmonary resuscitation	−14.193	<0.0001	−0.066	0.1511
Use of intra-aortic balloon pump	−2.625	0.0369	1.181	0.3702
Use of continuous renal replacement therapy	−33.990	<0.0001	−16.734	<0.0001
Use of mechanical ventilator	−26.906	<0.0001	−1.061	0.0853
Successful coronary revascularization	−8.659	0.0047	−3.370	0.0316
Staged percutaneous coronary intervention	−5.172	0.0135	0.500	0.2365

AIC indicates Akaike's information criterion.

pro-B-type natriuretic peptide score, which calculates the mortality caused by ischemic CS based on 4 simple laboratory markers.[19] This score demonstrated acceptable prognostic power (AUC, 0.83). However, critical weakness of laboratory marker-based scores lies in the limited availability of all 4 laboratory markers at every center and variability of laboratory results depending on the time of sampling and processing protocol.

The PRECISE score is composed of data on homogenous cause and reflects the reality of refractory ischemic CS by including all patients with AMI who received ECMO, regardless of ECPR or surgical revascularization. Our prediction equation may seem complicated compared with previous scores, which indicate a simple risk stratified by numeric scores. However, our equation provides a fairly accurate probability of mortality by using variables routinely available

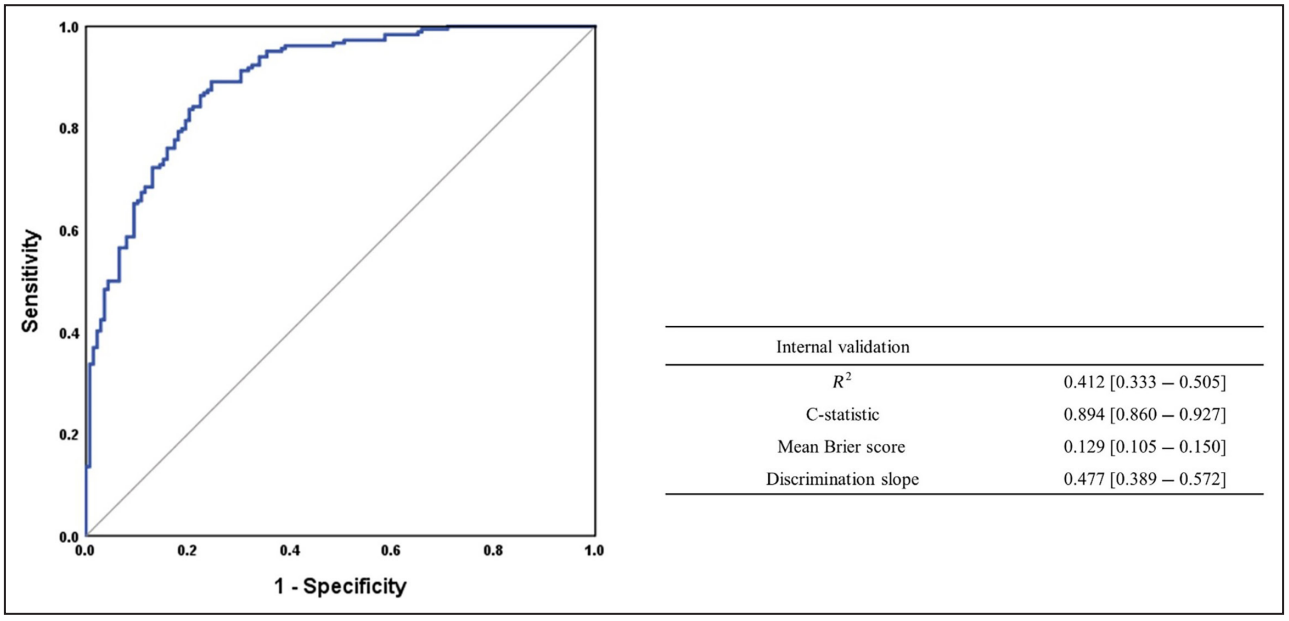


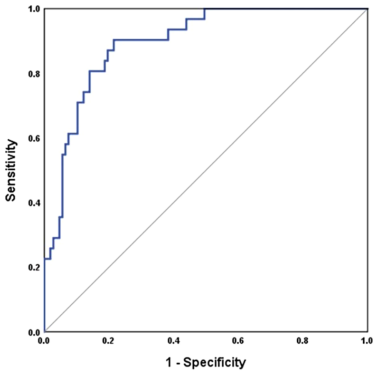
Figure 2. Prediction performance after internal validation.

A. The PRECISE score

(1) In-hospital death = exp(linear predictor) / [1+exp(linear predictor)]

(2) Linear predictor = 13.3759 - 0.0076 × (Age) - 0.0057 × (DBP) - 0.0695 × (Lowest LVEF) + 0.7519 × (Creatinine) + 0.2416 × (Peak lactic acid) - 0.00134 × (Vasoactive inotropic score) + 0.00015 × (Shock to ECMO time) - 1.2763 × (Hypertension) + 0.3564 × (CKD) -14.2562 × (Successful revascularization) + 1.2956 × (Staged PCI) + 0.6769 × (Use of IABP) + 0.1661 × (ECPR) - 18.9556 × (Use of CRRT) - 0.7773 × (Use of Mechanical ventilator) + 0.0061 × (Age) × (Peak lactic acid) -0.0498 × (Age) × (ECPR) + 0.0498 × (Age) × (Use of CRRT) + 0.0842 × (Lowest LVEF) × (ECPR) - 0.4271 × (Creatinine) × (CKD) - 0.4242 × (Creatinine) × (Use of CRRT) + 0.2164 × (Peak lactic acid) × (Hypertension) - 0.6107 × (Peak lactic acid) × (Successful revascularization) + 17.8809 × (Successful revascularization) × (Use of CRRT) -2.9114 × (Use of IABP) × (ECPR)

B. ROC curve after external valiation



External validation	
R^2	0.487 [0.398 – 0.582]
C-statistic	0.895 [0.853 – 0.930]
Mean Brier score	0.112 [0.087 – 0.134]
Discrimination slope	0.373 [0.257 – 0.487]

Figure 3. The PRECISE score and prediction performance after external validation.
A, Final prediction equation of the PRECISE score after calibration, **B**, Area under the receiver operating characteristic curve of the PRECISE score after external validation. The units or ranges of continuous predictors were age (years), diastolic blood pressure (mm Hg), lowest LVEF (%), serum creatinine (mg/dL), peak lactic acid level (mmol/L), vasoactive-inotropic score, and shock to ECMO insertion time (min). Binary predictors of hypertension, chronic kidney disease, ECPR, use of IABP, use of CRRT, use of a mechanical ventilator, successful coronary revascularization, and staged PCI were coded as 1 (yes) or 0 (no). CKD indicates chronic kidney disease; CRRT, continuous renal replacement therapy; DBP, diastolic blood pressure; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PRECISE, Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support; and ROC, receiver operating characteristic.

in real-world practice. Moreover, the PRECISE score was successfully validated using independent, prospective data.

Interpretation of the PRECISE Score

Based on the AIC statistics, 15 clinically significant variables were selected as predictors of the PRECISE score. Age is one of the strongest nonmodifiable risk factors for cardiovascular mortality. In addition, chronic illnesses such as hypertension and chronic kidney disease were included as nonmodifiable risk factors for shock. “Use of CRRT” not only implies acute renal impairment, but it also reflects the severity of hypoperfusion during shock. Similarly, several indices that implied the degree of hypoperfusion were included: lactic acid and creatinine levels, LVEF, vasoactive inotropic score, and shock to ECMO time.[23] Clinical indices such as creatinine and lactic acid levels and LVEF were monitored serially to evaluate the degree of hypoperfusion. By choosing the worst value of each index (creatinine at the presentation of shock, peak lactic acid level, and lowest LVEF), we aimed to reflect the most severe period during shock. In addition, because the PRECISE score was developed to estimate outcomes in patients with AMI, we also included the severity of coronary artery disease and its reperfusion. Successful revascularization of the culprit lesion is critical for shock recovery, and whether PCI should be performed immediately or staged is also important. Although staged PCI is not common in clinical practice (5.0% of the total cohort), patients who underwent staged PCI might have had less severe coronary artery disease with improved perfusion. Additionally, the presence of ECPR and organ failure parameters (use of a mechanical ventilator, CRRT, and IABP) were also included as powerful predictors of in-hospital mortality.

Compared with the developmental data, the external data revealed significant differences in mortality and baseline characteristics. The major reason for the significant difference between the 2 data sets is the different characteristics of the participating hospitals.

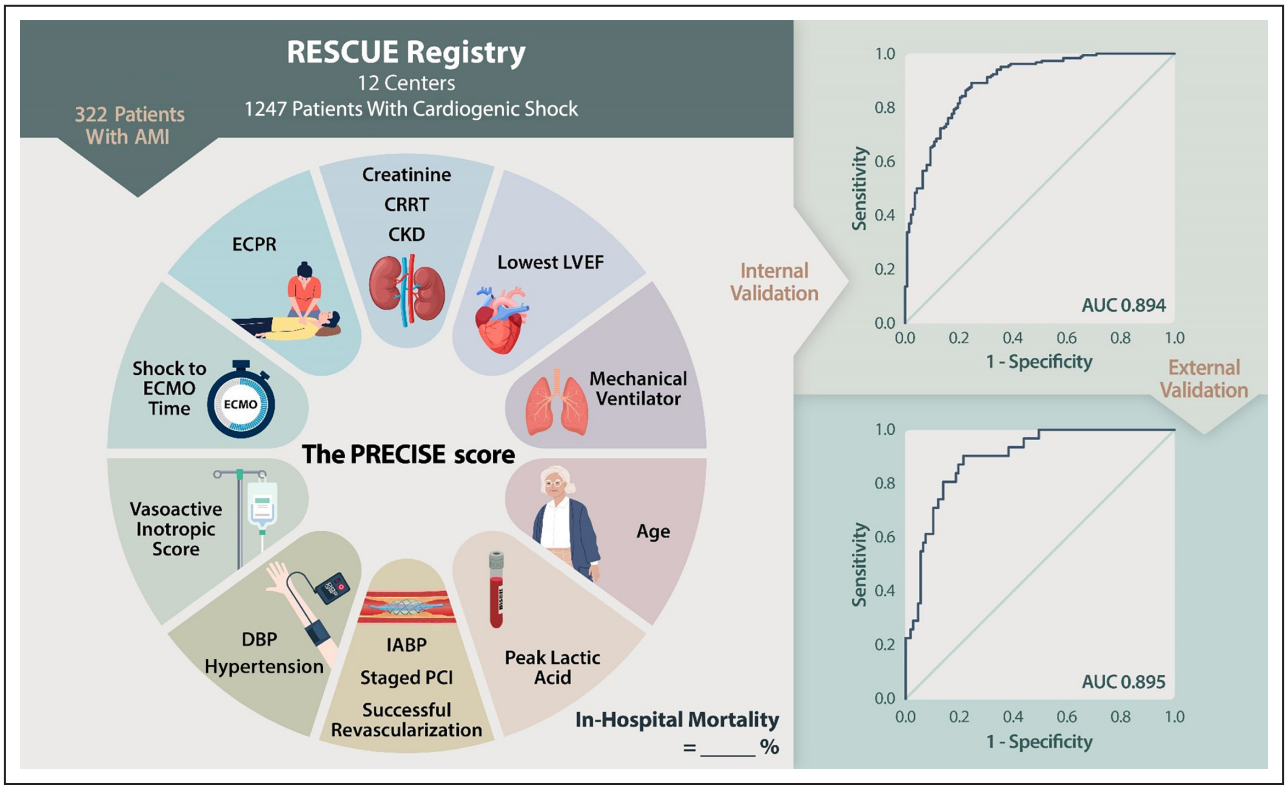


Figure 4. Development of the PRECISE score for refractory ischemic cardiogenic shock requiring ECMO support.
The PRECISE score was developed to predict in-hospital mortality owing to refractory ischemic cardiogenic shock requiring ECMO support. The prediction equation was as follows: The PRECISE-score was internally and externally validated using prospective data. The online calculator is available at www.theprecisescore.com. AMI indicates acute myocardial infarction; AUC, area under the receiver operating characteristic; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; DBP, diastolic blood pressure; ECMO, extracorporeal membrane oxygenation; ECPR, extracorporeal cardiopulmonary resuscitation; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; PRECISE, Prediction of In-Hospital Mortality for Patients With Refractory Ischemic Cardiogenic Shock Requiring Veno-Arterial Extracorporeal Membrane Oxygenation Support; and RESCUE, Retrospective and Prospective Observational Study to Investigate Clinical Outcomes and Efficacy of Left Ventricular Assist Device for Korean Patients With Cardiogenic Shock.

The developmental cohort included 12 tertiary centers that reflected different properties: national hospitals, private hospitals, and hospitals located in various regions. More important, several centers were designated as regional emergency medical centers that mandated accommodating any referred patients in that region. The administrative obligations of regional emergency medical centers may have resulted worse outcomes in critically ill patients. Conversely, the external cohort was derived from a single center that was experienced in ECMO management and was not designated as a regional emergency medical center. Therefore, the different hospital characteristics influenced the outcomes and baseline characteristics of the data. The PRECISE score was developed on a multicenter registry that included patients with severe disease and was successfully calibrated in the validation registry of patients with milder disease, implicating its extensive applicability in a broad range of patients with refractory ischemic CS.

Clinical Implication

Although the PRECISE score was developed for clinical use, it was not designed to determine whether ECMO should be administered. In fact, decision to deploy ECMO is determined by weighing indications, contraindications, and relevant clinical situations and available resources, rather than by expected probability of survival measured at the onset of shock.[24] In addition, recent result from the ECLS-SHOCK (Extracorporeal Life Support in Cardiogenic Shock) trial has revealed nonsuperiority of early routine ECMO support in patients with AMI complicated by CS.[6] That is, even after initiation of ECMO support, it does not guarantee optimistic outcome in all patients and is associated with various complications. Prolonged maintenance of ECMO also involves a significant burden of health expenditures and resources. The PRECISE score features its maximal utility when all the 15 predictors are obtained—which would be after coronary revascularization, ECMO insertion, and use of vasoactive agents

within the first 48 hours of shock. If short-term recovery is not expected in patients with ECMO support, the PRECISE score may be used as supportive evidence for further decision-making processes, such as (1) alteration to durable ventricular assist device or heart transplantation, (2) decision to further invasive procedures (ie, left ventricular venting maneuver, and central cannulation), or (3) withdrawal of ECMO support.[25] The value of the PRECISE score lies in supporting further clinical decisions that matter in the latter phase of CS management.

Limitations

This study had several limitations. First, the PRECISE score could not be directly compared with other prediction models. Use and comparison of other scores necessitates additional variables (ie, peak inspiratory pressure for calculation of the survival after venoarterial-ECMO score, prothrombin activity for the calculation of the Prediction of Cardiogenic Shock Outcome for AMI Salvaged by Veno-arterial ECMO score), which is practically difficult if they are not obtained in a prospective manner. Further validation and comparison with other prediction models might improve its clinical utility. Second, there may have been several biases due to the retrospective nature of the cohort. For developmental data, missing data were imputed, and for external validation data, patients with missing values were excluded. This might have resulted in survivor bias: excluding patients with more severe disease who did not survive until coronary angiography or revascularization. Third, our study is focused on patients who required ECMO support, and applying the PRECISE score to other mechanical circulatory supports may be limited. Short-term mechanical circulatory supports other than ECMO, such as Impella or TandemHeart, are not available in Korea.[26] Similarly, use of implantable left ventricular assist devices were not covered by Korean national insurance until September 2018. Lastly, the RESCUE registry is a CS registry that is limited to East Asian population, exclusively confined to South Korean citizens. The clinical characteristics and outcomes may differ significantly between Asian patients with CS and the non-Asian population. Further validation studies are required in non-Asian patients with CS.

CONCLUSIONS

The PRECISE score is a systematic prediction model for patients with refractory ischemic CS who require ECMO insertion. The probability of mortality was predicted using routinely available parameters before and after ECMO insertion that were highly predictive. The PRECISE score can be used in patients with refractory ischemic CS to provide prognostic information and establish further treatment strategies in the critical phase of CS.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S7.
Figures S1–S2.

REFERENCES

1. Thiele H, Allam B, Chatellier G, Schuler G, Lafont A. Shock in acute myocardial infarction: the Cape Horn for trials? *Eur Heart J*. 2010;31:1828–1835. doi: 10.1093/eurheartj/ehq220
2. Thiele H, Ohman EM, de Waha-Thiele S, Zeymer U, Desch S. Management of cardiogenic shock complicating myocardial infarction: an update 2019. *Eur Heart J*. 2019;40:2671–2683. doi: 10.1093/eurheartj/ehz363
3. Aso S, Matsui H, Fushimi K, Yasunaga H. In-hospital mortality and successful weaning from venoarterial extracorporeal

membrane oxygenation: analysis of 5263 patients using a national inpatient database in Japan. *Crit Care*. 2016;20:80. doi: 10.1186/s13054-016-1261-1
4. Combes A, Leprince P, Luyt CE, Bonnet N, Trouillet JL, Léger P, Pavie A, Chastre J. Outcomes and long-term quality-of-life of patients supported by extracorporeal membrane oxygenation for refractory cardiogenic shock. *Crit Care Med*. 2008;36:1404–1411. doi: 10.1097/CCM.0b013e31816f7cf7
5. Harjola VP, Lassus J, Sionis A, Køber L, Tarvasmäki T, Spinar J, Parissis J, Banaszewski M, Silva-Cardoso J, Carubelli V, et al. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail*. 2015;17:501–509. doi: 10.1002/ejhf.260
6. Thiele H, Zeymer U, Akin I, Behnes M, Rassaf T, Mahabadi AA, Lehmann R, Eitel I, Graf T, Seidler T, et al. Extracorporeal life support in infarct-related cardiogenic shock. *N Engl J Med*. 2023;389:1286–1297. doi: 10.1056/NEJMoa2307227
7. Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT, Hodgson C, Scheinkestel C, Cooper DJ, Thiagarajan RR, et al. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J*. 2015;36:2246–2256. doi: 10.1093/eurheartj/ehv194
8. Muller G, Flecher E, Lebreton G, Luyt CE, Trouillet JL, Brechot N, Schmidt M, Mastroianni C, Chastre J, Leprince P, et al. The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock. *Intensive Care Med*. 2016;42:370–378. doi: 10.1007/s00134-016-4223-9
9. Wang L, Yang F, Wang X, Xie H, Fan E, Ogino M, Brodie D, Wang H, Hou X. Predicting mortality in patients undergoing VA-ECMO after coronary artery bypass grafting: the REMEMBER score. *Crit Care*. 2019;23:11. doi: 10.1186/s13054-019-2307-y
10. Park SB, Yang JH, Park TK, Cho YH, Sung K, Chung CR, Park CM, Jeon K, Song YB, Hahn JY, et al. Developing a risk prediction model for survival to discharge in cardiac arrest patients who undergo extracorporeal membrane oxygenation. *Int J Cardiol*. 2014;177:1031–1035. doi: 10.1016/j.ijcard.2014.09.124
11. Butala N, Yamga E, Rosen D, Bucholz E, Yeh RW, Celi LA, Ustun B. Optimized risk score to predict mortality in patients with cardiogenic shock in the cardiac intensive care unit. *J Am Coll Cardiol*. 2022;79:246. doi: 10.1016/S0735-1097(22)01237-2
12. Yang JH, Choi KH, Ko YG, Ahn CM, Yu CW, Chun WJ, Jang WJ, Kim HJ, Kim BS, Bae JW, et al. Clinical characteristics and predictors of in-hospital mortality in patients with cardiogenic shock: results from the RESCUE registry. *Circ Heart Fail*. 2021;14:e008141. doi: 10.1161/CIRCHEARTFAILURE.120.008141
13. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS, White HD, et al. Third universal definition of myocardial infarction. *Eur Heart J*. 2012;33:2551–2567. doi: 10.1093/eurheartj/ehs184
14. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. *Circulation*. 2013;127:e362–e425. doi: 10.1161/CIR.0b013e3182742cf6
15. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, Charpie JR, Hirsch JC. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med*. 2010;11:234–238. doi: 10.1097/PCC.0b013e3181b806fc
16. Steyerberg EW. *Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating*. Springer; 2019:63–75. doi: 10.1007/978-3-030-16399-0
17. Steyerberg EW, Harrell FE Jr. Prediction models need appropriate internal, internal-external, and external validation. *J Clin Epidemiol*. 2016;69:245–247. doi: 10.1016/j.jclinepi.2015.04.005
18. Steyerberg EW, Harrell FE Jr, Borsboom GJ, Eijkemans MJ, Vergouwe Y, Habbema JD. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol*. 2001;54:774–781. doi: 10.1016/s0895-4356(01)00341-9
19. Ceglarek U, Schellong P, Rosolowski M, Scholz M, Willenberg A, Kratzsch J, Zeymer U, Fuernau G, de Waha-Thiele S, Buttner P, et al. The novel cystatin C, lactate, interleukin-6, and N-terminal pro-B-type natriuretic peptide (CLIP)-based mortality risk score in cardiogenic shock after acute myocardial infarction. *Eur Heart J*. 2021;42:2344–2352. doi: 10.1093/eurheartj/ehab110
20. Shah M, Patnaik S, Patel B, Ram P, Garg L, Agarwal M, Agrawal S, Arora S, Patel N, Wald J, et al. Trends in mechanical circulatory support use and hospital mortality among patients with acute myocardial infarction and non-infarction related cardiogenic shock in the United States. *Clin Res Cardiol*. 2018;107:287–303. doi: 10.1007/s00392-017-1182-2
21. Karagiannidis C, Brodie D, Strassmann S, Stoelben E, Philipp A, Bein T, Muller T, Windisch W. Extracorporeal membrane oxygenation: evolving epidemiology and mortality. *Intensive Care Med*. 2016;42:889–896. doi: 10.1007/s00134-016-4273-z
22. Chang K, Ahn Y, Lim S, Yang JH, Lee KY, Choo EH, Kim HK, Nam CW, Kim W, Hwang JY, et al. 2021 Korean Society of Myocardial Infarction Expert Consensus Document on revascularization for acute myocardial infarction. *Korean Circ J*. 2021;51:289–307. doi: 10.4070/kcj.2021.0043
23. Jentzer JC, Schrage B, Patel PC, Kashani KB, Barsness GW, Holmes DR, Blankenberg S, Kirchhof P, Westermann D. Association between the Acidemia, lactic acidosis, and shock severity with outcomes in patients with cardiogenic shock. *J Am Heart Assoc*. 2022;11:e024932. doi: 10.1161/JAHA.121.024932
24. Keebler ME, Haddad EV, Choi CW, McGrane S, Zalawadiya S, Schlendorf KH, Brinkley DM, Danter MR, Wigger M, Menachem JN, et al. Venoarterial extracorporeal membrane oxygenation in cardiogenic shock. *JACC Heart Fail*. 2018;6:503–516. doi: 10.1016/j.jchf.2017.11.017
25. van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, Kilic A, Menon V, Ohman EM, Sweitzer NK, et al. Contemporary Management of Cardiogenic Shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232–e268. doi: 10.1161/CIR.0000000000000525
26. Hyun J, Cho JY, Youn JC, Kim D, Cho DH, Park SM, Jung MH, Cho HJ, Park SM, Choi JO, et al. Korean Society of Heart Failure Guidelines for the Management of Heart Failure: advanced and acute heart failure. *Korean Circ J*. 2023;53:452–471. doi: 10.4070/kcj.2023.0115