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NEW RESEARCH PAPERS

FOCUS ON SHOCK AND ACUTE CORONARY SYNDROMES

Resuscitation Using ECPR During In-Hospital Cardiac Arrest (RESCUE-IHCA) Mortality Prediction Score and External Validation

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ABSTRACT

OBJECTIVES The aim of this study was to develop and validate a score to accurately predict the probability of death for adult extracorporeal cardiopulmonary resuscitation (ECPR).

BACKGROUND ECPR is being increasingly used to treat refractory in-hospital cardiac arrest (IHCA), but survival varies from 20% to 40%.

METHODS Adult patients with extracorporeal membrane oxygenation for IHCA (ECPR) were identified from the American Heart Association GWTG-R (Get With the Guidelines-Resuscitation) registry. A multivariate survival prediction model and score were developed to predict hospital death. Findings were externally validated in a separate cohort of patients from the Extracorporeal Life Support Organization registry who underwent ECPR for IHCA.

RESULTS A total of 1,075 patients treated with ECPR were included. Twenty-eight percent survived to discharge in both the derivation and validation cohorts. A total of 6 variables were associated with in-hospital death: age, time of day, initial rhythm, history of renal insufficiency, patient type (cardiac vs noncardiac and medical vs surgical), and duration of the cardiac arrest event, which were combined into the RESCUE-IHCA (Resuscitation Using ECPR During IHCA) score. The model had good discrimination (area under the curve: 0.719; 95% CI: 0.680-0.757) and acceptable calibration (Hosmer and Lemeshow goodness of fit $P = 0.079$). Discrimination was fair in the external validation cohort (area under the curve: 0.676; 95% CI: 0.606-0.746) with good calibration ($P = 0.66$), demonstrating the model's ability to predict in-hospital death across a wide range of probabilities.

CONCLUSIONS The RESCUE-IHCA score can be used by clinicians in real time to predict in-hospital death among patients with IHCA who are treated with ECPR. (J Am Coll Cardiol Intv 2022;15:237–247) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

ECMO = extracorporeal membrane oxygenation

ECPR = extracorporeal cardiopulmonary resuscitation

ELSO = Extracorporeal Life Support Organization

IHCA = in-hospital cardiac arrest

OHCA = out-of-hospital cardiac arrest

ROSC = return of spontaneous circulation

Extracorporeal cardiopulmonary resuscitation (ECPR) is increasingly used worldwide as a rescue technique among patients with refractory cardiac arrest (1). ECPR is used to rescue patients who arrest in-hospital and those with out-of-hospital cardiac arrest (OHCA) brought to the emergency department. As a component within a bundle of interventions for OHCA due to refractory ventricular fibrillation, ECPR was recently shown to be highly effective in improving survival and producing good neurologic outcomes compared with conventional cardiopulmonary resuscitation in a randomized controlled trial (2). Although randomized controlled trials demonstrating the effectiveness of ECPR in in-hospital cardiac arrest (IHCA) are lacking, observational studies have reported 20% to 40% survival (3,4). However, there is large variation in this survival benefit, highlighting the importance of patient selection (5). Information on patient factors associated with improved survival with ECPR remains limited but important to understand given the associated complications and cost and resources needed to deliver ECPR care (6-8).

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Models to predict survival in patients receiving extracorporeal membrane oxygenation (ECMO) have been developed in patients with cardiogenic shock and respiratory failure (9,10). However, ECMO for IHCA (ie, ECPR) represents a unique clinical condition in which survival is likely dependent on resuscitation-specific variables such as the duration of resuscitative efforts (11). Prior studies of inpatient ECPR are limited by small sample size and limited generalizability due to the inclusion of a small number of sites (12).

To address this gap in knowledge, we conducted a large national study of ECPR among 1,075 patients from 219 centers participating in the GWTG-R (Get With the Guidelines-Resuscitation) registry to develop a mortality prediction model using simple baseline and arrest characteristics and display the results with a simple-to-calculate score. The model was designed to be used by clinicians in real time for use in patients who receive ECPR to treat their IHCA to inform their probability of death. We externally validated our model in a separate cohort of ECPR patients from the Extracorporeal Life Support Organization (ELSO) registry.

METHODS

Our analysis is reported according to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis guideline and incorporated best practice recommendations for variable selection and model construction when using existing observational datasets, including reporting model calibration, prediction accuracy, checking for overfitting, and external validation (Supplemental Appendix). Analysis was approved by the Institutional Review Board at the University of Utah (#91962).

DATA SOURCE. Data were obtained from the American Heart Association GWTG-R registry. Briefly, patients are defined as having IHCA if they have lack of pulse, apnea, and unresponsiveness, without do-not-resuscitate orders, and subsequently receive chest compressions and cardiopulmonary resuscitation or defibrillation. Registry details are provided in the Supplemental Appendix.

STUDY POPULATION. We identified inpatient cardiac arrest events from 2000 to 2018 that were treated with ECPR as part of the arrest. This population has been previously described in detail (5) and is described in the Supplemental Appendix. Briefly, we excluded patients <18 years of age and those with OHCA preceding admission. We excluded all non-index cardiac arrest events for each patient, patients from hospitals that had submitted <6 months of data or fewer than 5 cardiac arrest events submitted to the GWTG-R registry, and patients with missing neurologic outcome data.

EXTERNAL VALIDATION COHORT. The validation cohort was obtained from patients entered into the ELSO registry during 2017. Registry details are provided in the Supplemental Table 1, but briefly, patients were included if they were ≥18 years of age, had IHCA during admission, did not have OHCA prior to admission, and had been decannulated from ECMO (Supplemental Table 2). Patients overlapping between the ELSO and GWTG-R registries were

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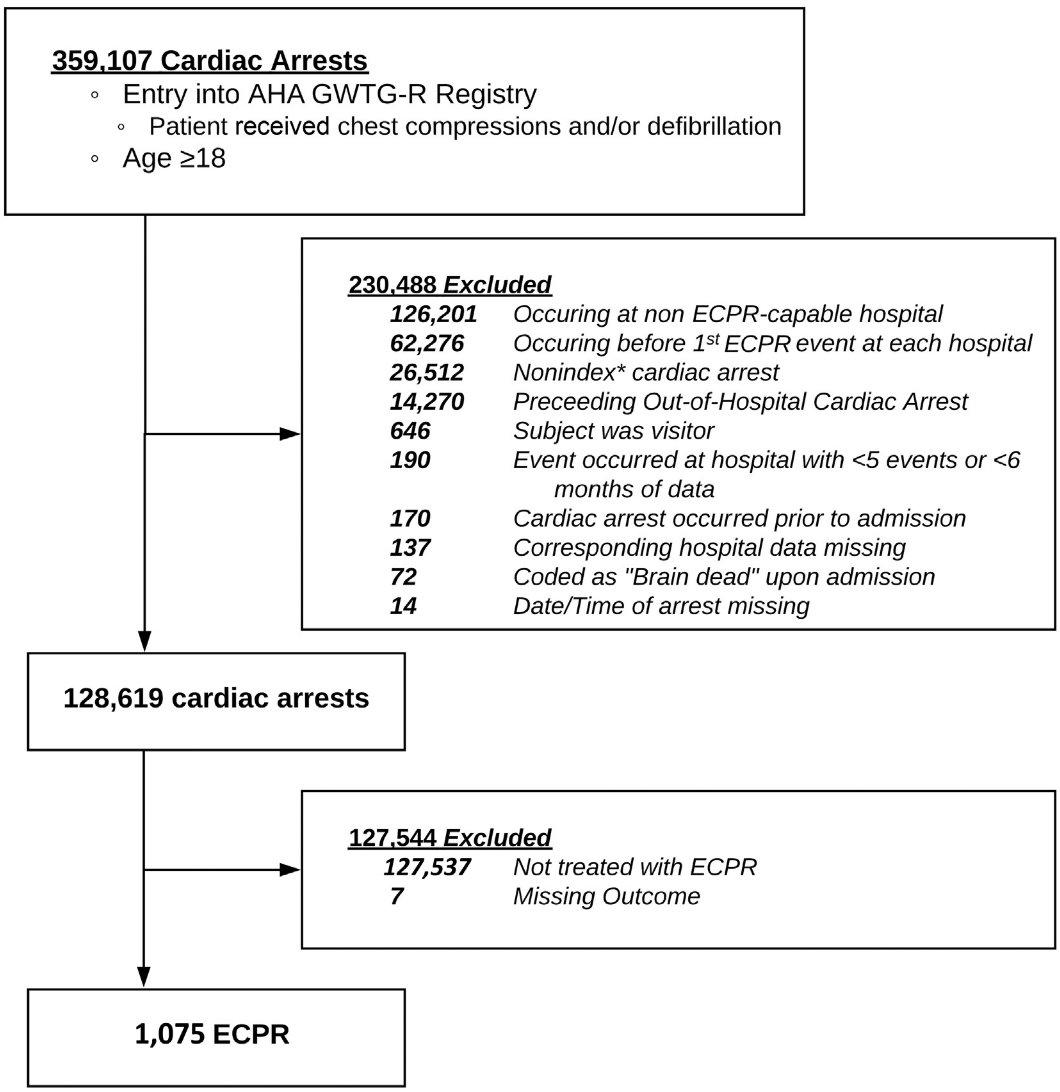
FIGURE 1 **Study Enrollment Flowchart**



Patients with in-hospital cardiac arrest from the American Heart Association (AHA) GWTG-R (Get With the Guidelines–Resuscitation) registry treated with extracorporeal cardiopulmonary resuscitation (ECPR). Patients with prior out-of-hospital cardiac arrest, nonindex arrest, or missing outcome data were excluded, as were patients who arrested at a hospital at which ECPR had not previously been performed. *Cardiac arrests that were not the first cardiac arrest per patient during the current admission.

identified through previously described linkage using these 2 datasets (13) and were excluded from the validation dataset.

STUDY OUTCOME AND VARIABLES. Our primary outcome was in-hospital death. Candidate predictor variables selected a priori included patient and arrest characteristics previously associated with survival after both cardiac arrest and/or ECMO. These variables are listed in detail in the Supplemental Appendix and broadly included demographics, initial arrest rhythm, patient type, location of cardiac arrest, time of day and day of week of cardiac arrest, comorbid medical conditions prior to arrest, therapeutic interventions in place at the time of cardiac arrest, and intra-arrest characteristics and treatments. Handling of missing data is described in the Supplemental Appendix.

STATISTICAL ANALYSIS. Potential predictors were summarized descriptively stratified by discharge survival status. Continuous variables were

TABLE 1 Patient Characteristics

	Dead (n = 769)	Alive (n = 306)	*P* Value
Age (y)	61 (48-72)	58 (47-68)	0.019
Sex			
Male	467 (71)	195 (29)	0.36
Female	302 (73)	111 (27)	
Race			
White	547 (69)	249 (31)	<0.001
Non-White	219 (79)	57 (21)	
Hispanic ethnicity			
No	726 (71)	294 (29)	0.26
Yes	43 (78)	12 (22)	
Weight (kg)	80 (67-97)	78 (68-93)	0.49
Pre-existing conditions			
Hypoperfusion prior to arrest			
No	418 (69)	186 (31)	0.06
Yes	348 (74)	120 (26)	–
Stroke or neurologic disorder			
No	695 (72)	277 (28)	0.92
Yes	71 (71)	29 (29)	–
Congestive heart failure			
No	493 (70)	216 (30)	0.052
Yes	273 (75)	90 (25)	–
Diabetes mellitus			
No	587 (71)	240 (29)	0.53
Yes	179 (73)	66 (27)	–
Hepatic insufficiency			
No	722 (71)	297 (29)	0.06
Yes	44 (83)	9 (17)	–
Major trauma			
No	733 (71)	299 (29)	0.11
Yes	33 (82)	7 (18)	–
Cancer			
No	732 (71)	299 (29)	0.10
Yes	34 (83)	7 (17)	–
Myocardial infarction (history)			
No	606 (72)	238 (28)	0.63
Yes	160 (70)	68 (30)	–
Myocardial infarction (this admission)			
No	558 (71)	225 (29)	0.82
Yes	208 (72)	81 (28)	–
Renal insufficiency			
No	573 (69)	257 (31)	0.001
Yes	193 (80)	49 (20)	–
Sepsis			
No	699 (71)	287 (29)	0.17
Yes	67 (78)	19 (22)	–
Devices already in place at time of arrest			
Mechanical ventilation			
No	384 (74)	138 (26)	0.15
Yes	384 (70)	168 (30)	–
Invasive airway			
No	400 (73)	146 (27)	0.20
Yes	368 (70)	160 (30)	–
Arterial catheter			
No	432 (72)	167 (28)	0.62
Yes	336 (71)	139 (29)	–
Time of day of arrest			
7 AM to 2:59 PM	332 (67)	166 (33)	<0.001
3 PM to 10:59 PM	262 (74)	93 (26)	–
11 PM to 5:59 AM	148 (85)	27 (15)	–

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summarized as median (IQR), and categorical variables were summarized as frequency and row percentage. Univariable comparisons of each predictor between survivors and nonsurvivors were done using Wilcoxon rank sum tests for continuous variables and chi-square tests for categorical variables. Variables associated with survival with *P* values $\leq$0.10 in univariate analyses were included in the final multivariable model. Variable multicollinearity was then checked among candidate predictors using a variable inflation factor. We intentionally excluded race from the prediction model to avoid encouraging racial bias in the use of ECPR, given that race is often a surrogate for unmeasured variables such as socioeconomic status.

A multivariable model predicting survival was developed using Bayesian model averaging after multiple imputation (14). Briefly, 20 augmented datasets were generated in which missing variables were imputed using regression methods in the R package MICE (15) (Supplemental Table 3). Bayesian model averaging was performed on each of the imputed datasets, and the models were combined to form a final prediction model in which coefficients were averaged across the 20 models (Supplemental Table 4). Model accuracy was assessed as area under the curve (AUC). Bootstrapping was used to construct 95% CIs for the odds ratios. A score to predict the probability of survival was then constructed to allow individual predictions without the need for model refitting (Supplemental Table 5). A Hosmer-Lemeshow test was conducted for the final model to assess model goodness of fit (16). Predicted values for death were categorized into quintiles and plotted versus their observed values, along with a goodness-of-fit line. A *P* value $>$ 0.05 suggests acceptable model fit. Finally, as patients who arrested in the operating room may have been characteristically different from other patients, some of whom included cardiac surgery patients who had access to cardiopulmonary bypass, a sensitivity analysis was done to describe differences between cardiac surgical patients and other patients and then to exclude patients who arrested in the operating room (Supplemental Appendix). The final model was then externally validated using data on patients $\geq$18 years of age from the ELSO registry who were treated with ECPR. Variable matching and categorization for external validation are presented in the Supplemental Appendix.

Odds ratios, 95% CIs, and *P* values were reported from all models. Statistical analyses were conducted in R version 3.4, significance was assessed at the 0.05 level, and all tests were 2 tailed.

RESULTS

PATIENT CHARACTERISTICS. Among patients in the GWTG-R registry, 1,075 had cardiac arrest treated with ECMO and met criteria for analysis (Figure 1). Survivors (28% [n = 306]) were younger than nonsurvivors (58 years [IQR: 47-68 years] vs 61 years [IQR: 48-72 years]; $P = 0.019$) and were more likely to be of White race than non-White race (31% vs 21%; $P < 0.001$) but were otherwise similar in sex (29% vs 27% men; $P = 0.36$) and weight (78 kg [IQR: 68-93 kg] vs 80 kg [IQR: 67-97 kg]; $P = 0.26$) (Table 1). Survivors were less likely to have histories of preexisting renal insufficiency prior to arrest (20% vs 31%; $P < 0.001$) but had otherwise similar comorbidities.

Survivors were more likely to arrest between 7 AM and 2:59 PM compared with 3 PM and 10:59 PM or 11 PM and 6:59 AM (33% vs 26% vs 15%; $P < 0.001$) and were more likely to be located in procedural areas such as the operating room or the coronary catheterization laboratory or in the emergency department compared with general inpatient wards. There were no significant differences between survivors and nonsurvivors in the presence of preexisting invasive medical devices such as arterial lines or mechanical ventilation or in the use of mechanical chest compression.

MORTALITY PREDICTION. Among factors initially associated with mortality in univariate analysis, 6 remained in the final multivariable model (Figure 2, Supplemental Appendix), which included age, preexisting renal insufficiency, off-hours arrest (3 PM to 6:59 AM), noncardiac surgical patient type or medical patient type, initial arrest rhythm, and increasing duration of arrest (Central Illustration). The model had good discrimination, with an AUC of 0.719 (95% CI: 0.680-0.757), implying that the score could predict mortality with 72% accuracy. The aforementioned variables were combined to develop a score to predict hospital survival (Table 2), the resuscitation using ECPR during IHCA (RESCUE-IHCA) score. Points are assigned according to the 6 variables, from −15 ranging up to >40. A greater number of points correspond to a higher probability of death, which ranged from 0.22 to 0.99 (Figure 3). The summed points from each of the 6 variables would be used to determine the probability of death for a patient with IHCA treated with ECMO. Model calibration, to show how accurately the model fits the observed data, indicated acceptable fit (Hosmer and Lemeshow goodness of fit $P = 0.079$) (Figure 4). As goodness-of-fit can change with different bin sizes, other sizes were tested, without improvement in fit. Likewise, restriction of the data to 2010 to 2018 did not change model fit (AUC: 0.719; 95% CI: 0.671-0.767).

EXTERNAL VALIDATION. The predictive model was externally validated within 297 adult patients from

TABLE 1 Continued

	Dead (n = 769)	Alive (n = 306)	P Value
Day of week			
Weekday	629 (71)	260 (29)	0.21
Weekend	140 (75)	46 (25)	–
Patient type			
Outpatient	13 (72)	5 (28)	1.00
Emergency department	37 (71)	15 (29)	–
Other	719 (72)	286 (28)	–
Arrest location			
General inpatient[a]	74 (75)	25 (25)	0.002
Outpatient[b]	13 (81)	3 (19)	–
Cardiac/coronary unit	75 (73)	28 (27)	–
ICU	309 (78)	88 (22)	–
OR/coronary catheterization laboratory	272 (65)	148 (35)	–
Emergency department	26 (65)	14 (35)	–
Illness category			
Medical			
Noncardiac	104 (78)	30 (22)	<0.001
Cardiac	257 (78)	74 (22)	
Surgical			
Noncardiac	63 (74)	22 (26)	
Cardiac	345 (66)	180 (34)	
Automated/mechanical chest compressions			
No	452 (71)	189 (29)	0.81
Yes	140 (71)	56 (29)	–
Presenting cardiac rhythm			
Asystole	160 (76)	51 (24)	<0.001
PEA	305 (76)	96 (24)	–
pVT	63 (68)	30 (32)	–
VF	110 (60)	74 (40)	–
Palpable pulse initially	79 (70)	34 (30)	–
Any VF or pVT during arrest			
No	351 (72)	139 (28)	0.95
Yes	418 (71)	167 (29)	–
Any return of spontaneous circulation during arrest			
No	215 (100)	1 (0)	<0.001
Yes	552 (65)	302 (35)	–
Total duration before durable ROSC (min)	44 (20-80)	23 (10-44)	<0.001
Induced hypothermia			
No	523 (67)	257 (33)	0.74
Yes	74 (65)	39 (35)	–

Values are median (IQR) or n (%). Row percentages are shown. Missing values by group: race = 3/0; weight = 401/154; preexisting conditions: hypoperfusion = 3/0, cerebrovascular accident or neurologic disorder = 3/0, congestive heart failure = 3/0, diabetes mellitus = 3/0, hepatic insufficiency = 3/0, major trauma = 3/0, cancer = 3/0, history of myocardial infarction = 3/0, myocardial infarction this hospitalization = 3/0, renal insufficiency = 3/0, sepsis = 3/0; admission CPC = 178/47; devices: mechanical ventilation = 1/0, invasive airway = 1/0, arterial line = 1/0; time of day of arrest = 27/20; compression method mechanical = 177/61; presenting rhythm status = 52/21; any ROSC = 2/3; total duration before durable ROSC = 105/57; induced hypothermia = 172/10. [a]Includes adults arresting in the newborn unit. [b]Such as ambulatory same-day surgery units; includes rehabilitation.

CPC = Cerebral Performance Category; ICU = intensive care unit; OR = operating room; PEA = pulseless electric activity; pVT = pulseless ventricular tachycardia; ROSC = return of spontaneous circulation; VF = ventricular fibrillation.

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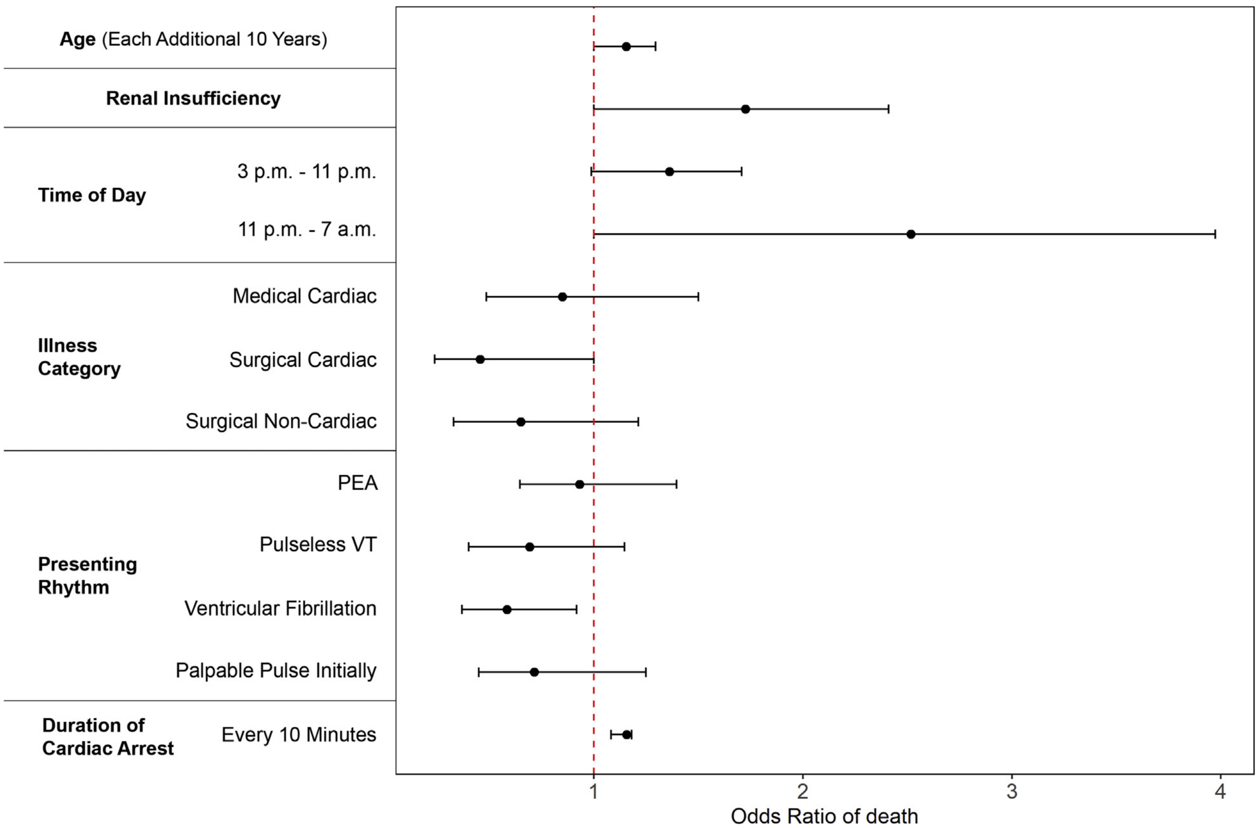
FIGURE 2 **Adjusted Odds of Individual Risk Factors With Death**



Adjusted association (odds ratio of death) for individual patient factors retained the multivariate mortality prediction model. PEA = pulseless electric activity; VT = ventricular tachycardia.

the ELSO registry who received ECMO for their cardiac arrest and met criteria for analysis (Supplemental Appendix). Patients were well matched on characteristics (**Table 3**) including survival, age, time of day of arrest, and duration of event. Despite differences in the characteristics of the validation cohort, the model discrimination was only marginally lower, with an AUC of 0.676 (95% CI: 0.606-0.746) compared with the derivation cohort. Model calibration likewise indicated acceptable fit (Hosmer and Lemeshow goodness-of-fit $P = 0.66$) (**Figure 5**). Other bin sizes were likewise tested without improvement in fit.

SENSITIVITY ANALYSIS. Sensitivity analysis excluding patients who arrested in the operating room excluded age as a predictive variable, but results were otherwise unchanged, with a similar AUC and acceptable calibration for both derivation and validation datasets (Supplemental Appendix, Supplemental Tables 6 to 8, Supplemental Figures 1 and 2).

TABLE 2 **Score Calculation**

	Points
Age	
≤20 y	2
Each additional 10 y	+2
Preexisting renal insufficiency	
Yes	+8
Time of day	
3 PM to 10:59 PM	+4
11 PM to 6:59 AM	+13
Illness category	
Medical cardiac	−2
Surgical cardiac	−11
Surgical noncardiac	−6
Presenting rhythm	
PEA	−1
pVT	−5
VF	−8
Palpable pulse initially	−5
Duration of cardiac arrest	
Each 10 min	+2

Abbreviations as in **Table 1**.

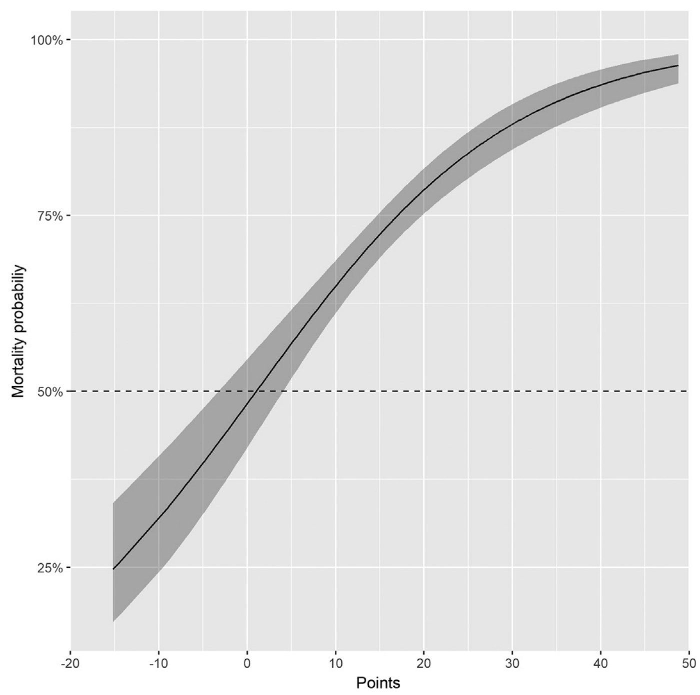
DISCUSSION

In this large study of hospitalized patients in the United States who sustained IHCA and were treated with ECPR, we identified 6 patient or arrest characteristics that were strongly associated with in-hospital mortality. These characteristics were combined to create the RESUCUE-IHCA score, a simple and easy to calculate score comprising only 6 variables, 5 of which can be obtained from the patient's history, without laboratory values. The RESCUE-IHCA can be used to determine an individual patient's estimated risk for mortality with good discrimination (AUC: 0.72) and calibration. The score was then externally validated in a separate cohort of 297 patients in the ELSO registry who received ECPR for IHCA. The calibration and validation values of the model show that the score can predict the probability of death with 72% accuracy. The score is simple and rapid enough to be used by clinicians at the beside.

Over the past decade, there has been a growing interest in the use of ECMO for adult cardiopulmonary failure, and cardiogenic shock after myocardial infarction (17-20). Although scores to predict outcomes in patients receiving ECMO have been previously reported, a vast majority of them are for patients receiving ECMO for nonarrest indications (eg, cardiogenic shock, severe respiratory failure) (9,10). Many require more variables and were not designed for ECPR (9,21,22); others lack external validation (23) or have lower accuracy (22,24,25). In 2020, Okada et al (23) analyzed 916 patients with OHCA. The Okada score had accuracy comparable with our RESCUE-IHCA score (AUC: 0.724 vs 0.719) but requires obtaining a laboratory value (pH), and external validation was not performed. Other scores from small sample sizes report high accuracy but lack validation and may be overfitted (26). External validation of prediction models on an external dataset is important, as it reflects the model's ability to generalize and is advised by best practice (27). Models that are internally validated may be overoptimistic or overfit (27,28). The RESCUE-IHCA score was derived from a large sample size of >1,000 adults from >200 hospitals treated with ECPR from a national dataset. The score externally validated across an international dataset of adults treated with ECPR for IHCA with good discrimination and calibration.

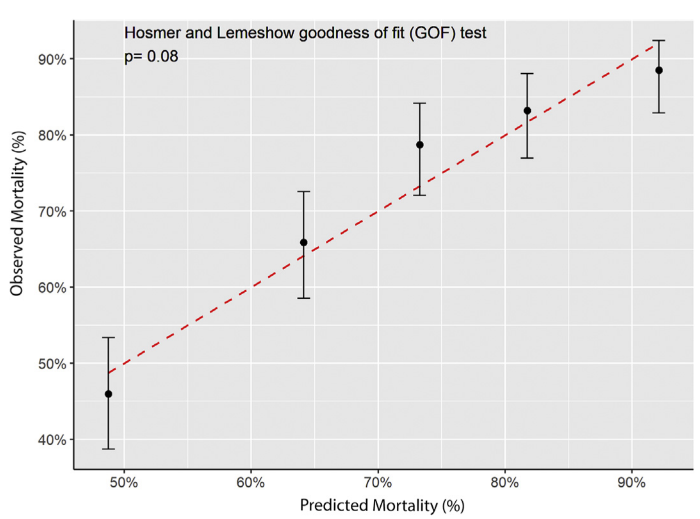
The RESCUE-IHCA score fills an important research gap, as the first large externally validated mortality prediction score for patients with IHCA treated with ECPR. The RESCUE-IHCA score enables a clinician to estimate at the bedside in real time, with 72% accuracy, a probability of death ranging from 22% to >99% using

FIGURE 3 Predicted Probability of Death Across Points



Curve with 95% CI shading showing the association between score points and mortality of in-hospital death among the derivation cohort.

FIGURE 4 Calibration Plot of Observed (y-Axis) Versus Predicted (x-Axis) Mortality From Derivation Dataset (GWTG-R Registry)



Discrimination and calibration of the model among 1,075 patients from the AHA GWTG-R registry. Correlation between observed mortality in the AHA GWTG-R dataset (y-axis) and predicted mortality according to the RESCUE-IHCA (Resuscitation Using ECPR During In-Hospital Cardiac Arrest) mortality prediction score (x-axis) in the derivation dataset. A *P* value >0.05 indicates acceptable fit. Abbreviations as in Figure 1.

TABLE 3 Comparison of Derivation and Validation Patient Characteristics

	Derivation (n = 1,075)	Validation (n = 297)	*P* Value
Age	60.0 (48.0-71.0)	59.1 (48.3-68.3)	0.58
Race			
White	796 (74)	155 (52)	<0.001
Non-White	276 (25.7)	142 (48)	–
Initial rhythm			
Asystole	211 (21)	24 (9)	<0.001
PEA	401 (40)	114 (41)	–
Pulseless ventricular tachycardia	93 (9)	34 (12)	–
Ventricular fibrillation	184 (18)	75 (27)	–
Palpable pulse initially	113 (11)	32 (12)	–
Time of day of arrest			
7:00 AM to 2:59 PM	498 (48)	138 (47)	0.73
3:00 PM to 10:59 PM	355 (35)	110 (37)	–
11:00 PM to 6:59 AM	175 (17)	49 (17)	–
Preexisting conditions			
Congestive heart failure	363 (34)	80 (27)	0.024
Renal insufficiency	242 (23)	76 (26)	0.28
Preceding hypoperfusion	468 (44)	271 (91)	<0.001
Duration of event, min	36.0 (17.0-69.0)	41.0 (27.0-60.0)	0.15
Patient type			
Medical noncardiac	134 (13)	66 (22)	<0.001
Medical cardiac	331 (31)	44 (15)	–
Surgical cardiac	525 (49)	138 (47)	–
Surgical noncardiac	85 (8)	49 (17)	–
Sustained ROSC	854 (80)	91 (31)	<0.001
Died	769 (72)	214 (72)	0.86

Values are median (IQR) or n (%). Missing values by group: race = 3/0, initial rhythm = 73/18, time of day = 47/0, congestive heart failure = 3/0, renal insufficiency = 3/0, hypoperfusion = 3/0, duration of event = 162/0, ROSC = 5/0.

Abbreviations as in Table 1.

patient characteristics known at the time of cardiac arrest, without waiting for laboratory values. Moreover, we found that 5 of the variables associated with survival were related to the conditions of the arrest or to the patient (age, patient type, history of renal insufficiency, time of day, and initial rhythm), whereas only 1 was a potentially modifiable intra-arrest feature (duration of arrest). This suggests that much of the probably of survival can be known on the basis of fixed characteristics of the patient and their arrest.

A striking finding is the influence of time of day on survival, with nocturnal ECPR conferring mortality risk comparable with renal insufficiency and older age. We previously demonstrated that US patients were more likely to receive ECPR for IHCA during daytime hours (5), reflecting increased staffing during the day. As such, this increased observed mortality at night may simply reflect fewer nighttime in-house staff members. We have previously shown that multiple specialties are involved in the care of ECPR patients (29) and that postarrest care is strongly correlated with survival (30), both of which may be more limited at night. These suggest that efforts to provide comparable levels of care at night for ECPR patients could improve survival. We note that the survival of patients during the weekend was 4% lower than during weekdays, which is the same as observed in previous analyses of cardiac arrest (31) but was not significant in our sample size, compared with the 15% improved daytime survival compared with night. Alternatively, the lower survival at night compared with the weekend may reflect slower psychomotor skills for this complex procedure, as has been suggested (32).

Although the RESCUE-IHCA score had modest calibration and discrimination, it was comparable with other scores derived from large registries for both ECMO without cardiac arrest and cardiac arrest without ECMO (33-36). The SAVE (Survival After Veno-Arterial-ECMO) score for cardiogenic shock treated with ECMO had an AUC of 0.68, while the RESP (Respiratory Extracorporeal Membrane Oxygenation Survival Prediction) score for respiratory failure treated with ECMO had an AUC of 0.74 (9,21). Many of the variables included in the RESCUE-IHCA score were also included in the CASPRI (Cardiac Arrest Survival Post-Resuscitation In-Hospital) score, which was developed for predicting survival with favorable neurologic outcomes for patients with IHCA (excluding ECMO) (37). However, the relative strength of association of individual variables with survival (eg, age, initial rhythm) differs between the 2 scores, given the inherent differences in patients treated with ECMO or ECPR compared with patients with IHCA not receiving these therapies (37). Many of the other scores require laboratory or other variables not routinely available for patients with OHCA treated with ECPR, a population in which our score validated. Our finding of worse outcomes with nocturnal ECPR is a new and important finding compared with previous ECMO scores.

We did note that the RESCUE-IHCA derivation cohort had a higher rate of return of spontaneous circulation (ROSC) (80% vs 31%) than the validation cohort, which is likely due to differences in definition of ROSC. Until 2015, the GWTG-R data collection form recorded any ROSC rather than ROSC sustained for longer than 20 minutes, as defined by ELSO and currently in the GWTG-R data.

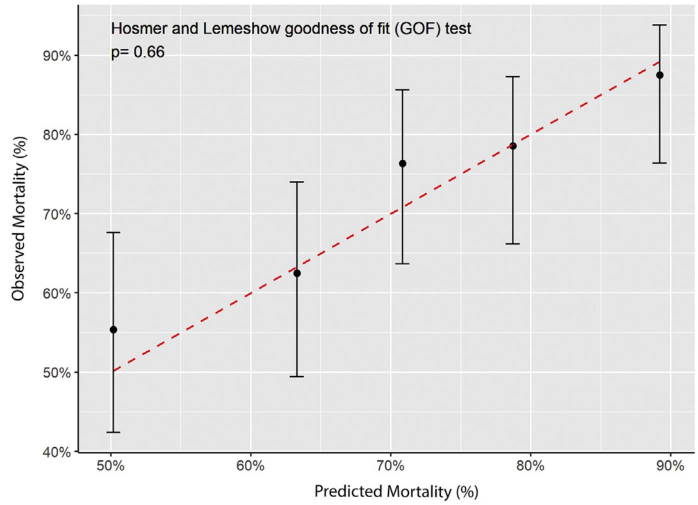
A strength of the RESCUE-IHCA score is that it can be calculated readily using 6 pre- and intra-arrest variables and does not include laboratory values; it is parsimonious compared with other survival prediction scores for either cardiac arrest or ECMO (9,21,22,37,38). We envision that the RESCUE-IHCA score would be of value to frontline physicians. By providing objective data with an externally validated model regarding the probability of death, the RESCUE-IHCA score can help clinicians engage with patients and their families as they navigate difficult decisions regarding goals of care in this resource-intensive, high-risk, and expanding population.

STUDY LIMITATIONS. First, although GWTG-R includes rich data on patient and cardiac arrest variables, data on variables such as quality of cardiopulmonary resuscitation prior to ECMO cannulation, laboratory values (eg, serum pH, lactate), and others that may be strongly associated with survival in this population were not available.

Second, we chose to predict hospital survival rather than neurologically intact survival. The GWTG-R data have a high proportion of missing neurologic status, which has been increasing in recent years. By choosing hospital mortality as our outcome, we were able to externally validate our score, a critical step; additionally, we observed that within our dataset, >85% of survivors had good neurologic outcomes recorded (Supplemental Table 9). This is consistent with the majority of other studies of adult ECPR, though it is a limitation we acknowledge, and future studies could examine neurologically intact survival as a relevant outcome.

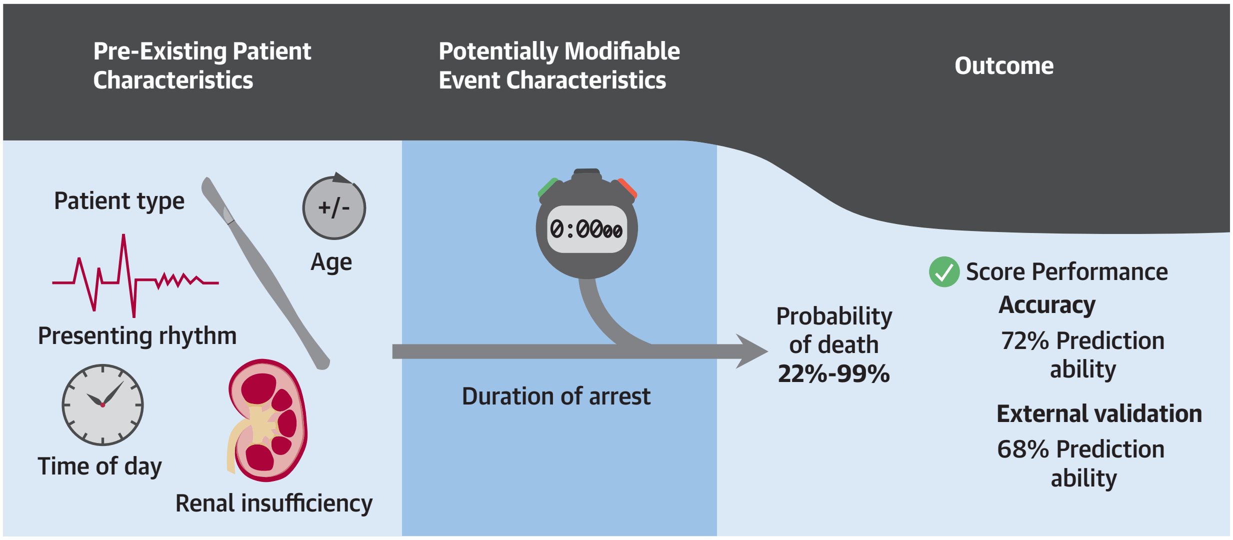
Our dataset included patients with IHCA, and as such, a large portion of our patients were cardiac

FIGURE 5 **Calibration Plot of Observed (y-Axis) Versus Predicted (x-Axis) Mortality From Validation Dataset (ELSO Registry)**



Discrimination and calibration from external validation among 297 patients with cardiac arrest treated with extracorporeal membrane oxygenation or ECPR from the ELSO (Extracorporeal Life Support Organization) registry. Correlation between observed mortality in the ELSO dataset (y-axis) and predicted mortality according to the RESCUE-IHCA mortality prediction score (x-axis) in the external validation dataset. A *P* value >0.05 indicates acceptable fit. Abbreviations as in Figures 1 and 4.

CENTRAL ILLUSTRATION **RESCUE-IHCA Score to Predict Hospital Mortality for Adult Extracorporeal Cardiopulmonary Resuscitation**



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The probability of hospital mortality for adult extracorporeal cardiopulmonary resuscitation (ECPR) can be accurately predicted with the RESCUE-IHCA (Resuscitation Using ECPR During In-Hospital Cardiac Arrest) score using 5 preexisting patient factors (age, time of day, initial rhythm, history of renal insufficiency, and patient type [cardiac vs noncardiac and medical vs surgical]) and 1 intra-arrest factor (duration of the cardiac arrest event). The score predicts the probability of mortality (ranging from 22% to 99%) with 72% accuracy and is externally validated with similar performance.

surgical patients. Although this may be considered a limitation, we have previously shown that this reflects the population in which ECPR is used for IHCA in the United States (5). Furthermore, the validation dataset from ELSO, the largest ECMO and ECPR registry in the world, reflected this patient type distribution also, suggesting that our model is well suited to the way in which ECPR has historically been used.

CONCLUSIONS

In this study, we developed and externally validated the RESCUE-IHCA score, a simple score that can be used at bedside to determine the probability of mortality in adult patients with IHCA treated with ECPR.

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PERSPECTIVES

WHAT IS KNOWN? No multicenter study with external validation has examined predictors of survival and mortality for adult ECPR.

WHAT IS NEW? The probability of death after IHCA treated with ECPR or ECMO can be rapidly predicted with good accuracy using only 6 patient and arrest characteristics without laboratory values: age, time of day, initial rhythm, history of renal insufficiency, patient type (cardiac vs noncardiac and medical vs surgical), and duration of the cardiac arrest event. The RESCUE-IHCA score is externally validated in the ELSO dataset with comparable accuracy.

WHAT IS NEXT? The RESCUE-IHCA score could be applied to patients with OHCA and modified using prearrest laboratory values to see how these influence score accuracy.

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KEY WORDS extracorporeal cardiopulmonary resuscitation, extracorporeal membrane oxygenation, in-hospital cardiac arrest, mortality prediction, survival prediction

APPENDIX For supplemental methods, tables, figures, and references, please see the online version of this paper.