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Authors
Tran, Andy T
Hart, Anthony J
Spertus, John A
et al.

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A Risk-Adjustment Model for Patients Presenting to Hospitals with Out-of-Hospital Cardiac Arrest and ST-Elevation Myocardial Infarction

Andy T. Tran, D.O., M.Sc.[a,b], **Anthony J. Hart, M.D.**[b,c], **John A. Spertus, M.D., M.P.H.**[b,c], **Philip G. Jones, M.S.**[b], **Bryan F. McNally, M.D., M.P.H.**[d,e], **Ali O. Malik, M.D., M.Sc.**[b,c], **Paul S. Chan, M.D., M.Sc.**[b,c]

a: Department of Medicine, University of California, Irvine School of Medicine, Orange, California, USA;

b: Saint Luke's Mid America Heart Institute, Kansas City, Missouri, USA;

c: University of Missouri–Kansas City, Kansas City, Missouri, USA;

d: Department of Emergency Medicine, Emory University School of Medicine, Atlanta, Georgia;

e: Rollins School of Public Health, Emory University, Atlanta, Georgia

Abstract

Background: Patients with ST-elevation myocardial infarction (STEMI) complicated by an out-of-hospital-cardiac-arrest (OHCA) may vary widely in their probability of dying. Large variation in mortality may have implications for current national efforts to benchmark operator and hospital mortality rates for coronary angiography. We aimed to build a risk-adjustment model of in-hospital mortality among OHCA survivors with concurrent STEMI.

Methods: Within the Cardiac Arrest Registry to Enhance Survival (CARES), we included adults with OHCA and STEMI who underwent emergent angiography within 2 hours of hospital arrival between January 2013 and December 2019. Using multivariable logistic regression to adjust for patient and cardiac arrest factors, we developed a risk-adjustment model for in-hospital mortality and examined variation in patients' predicted mortality.

Results: Of 2,999 patients (mean age 61.2 ±12.0, 23.1% female, 64.6% white), 996 (33.2%) died during their hospitalization. The final risk-adjustment model included higher age (OR per 10-year increase, 1.50 [95% CI: 1.39–1.63]), unwitnessed OHCA (OR, 2.51 [1.99–3.16]), initial non-shockable rhythm [OR, 5.66 [4.52–7.13]), lack of sustained pulse for >20 minutes (OR, 2.52 [1.88–3.36]), and longer resuscitation time (increased with each 10-minute interval) (c-statistic=0.804 with excellent calibration). There was large variability in predicted mortality: median, 25.2%, inter-quartile-range: 14.0% to 47.8%, 10th–90th percentile: 8.2 % to 74.1%.

Address for correspondence: Paul S. Chan, M.D., M.Sc., Saint Luke's Mid America Heart Institute, Cardiovascular Research, 4401 Wornall Rd, 9th Floor, Kansas City, MO 64111, USA; paulchan.mahi@gmail.com; Phone: 816-699-3409; Fax: 816-932-5613.

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Conclusions: In a large national registry, we identified 5 key predictors for mortality in patients with STEMI and OHCA and found wide variability in mortality risk. Our findings suggest that current national benchmarking efforts for coronary angiography, which simply adjusts for the presence of OHCA, may not adequately capture patient case-mix severity.

Classifications:

Post resuscitation care; acute coronary syndrome; outcome

Keywords

STEMI; cardiac arrest; risk adjustment; mortality; angiography; outcomes

INTRODUCTION

An estimated 5% of patients with ST-elevation myocardial infarction (STEMI) present with out-of-hospital cardiac arrest (OHCA), and these patients have as much as a 10-fold higher mortality rate as compared with STEMI patients without OHCA.[1] Consensus guidelines recommend emergent coronary angiography for OHCA patients with STEMI,[2–4] and meta-analysis of observational studies have reported better survival outcomes in patients with STEMI and OHCA who undergo early coronary angiography.[5] Although the mortality rate of patients with STEMI and OHCA, on average, is 27–30%,[1, 6] it is possible that predicted mortality risk varies widely.

In most patients with OHCA (the vast majority of whom do not have concurrent STEMI), the main predictors of survival include age, initial cardiac arrest rhythm, whether the OHCA was witnessed or received bystander cardiopulmonary resuscitation (CPR), location of cardiac arrest, total resuscitation time, and return of spontaneous circulation for at least 20 consecutive minutes (ROSC) prior to hospital arrival. However, the predictors for mortality in OHCA patients with STEMI may differ. Importantly, if there is substantial heterogeneity in mortality risk among patients who present with OHCA and STEMI, this may have significant implications for national efforts to benchmark operator and hospital mortality rates for coronary angiography, as current models only adjust for whether a patient had an OHCA as a binary variable and would not capture the heterogeneity of mortality risk for these high-risk patients.[7, 8]

Accordingly, within a national registry of OHCA, we created a parsimonious model to predict overall mortality in patients with OHCA and STEMI who were admitted at a hospital and underwent emergent coronary angiography. We then applied this model to the cohort and examined the distribution in predicted mortality risk to highlight how current risk-adjustment for the presence of OHCA as a binary variable may not fully capture patients' case-mix in national benchmarking for coronary angiography.

METHODS

Data Source and Study Design

The data used to conduct the research will be made available upon request and approval by CARES to any researcher for purposes of reproducing the results or replicating the procedure. The Cardiac Arrest Registry to Enhance Survival (CARES) is a prospective, multicenter registry of patients with OHCA in the U.S. established by the Centers for Disease Control and Emory University for public health surveillance and continuous quality improvement. The design of the registry has been previously described.[9, 10] Briefly, all patients with a confirmed OHCA (defined as pulselessness, apnea, and unresponsiveness) and for whom resuscitation is attempted are identified and followed by Emergency Medical Service (EMS) systems. CARES has a broad reach in the U.S., representing a catchment area of approximately 152 million residents or approximately 46% of the U.S. population in over 40 states. Data are collected from three sources that comprehensively define the continuum of emergency cardiac care: 911 dispatch centers, EMS agencies, and receiving hospitals. Standardized international Utstein definitions for specifying clinical variables and outcomes are used to ensure uniformity.[11] A CARES analyst reviews every record for completeness and accuracy.[10]

CARES collects patient-level data on demographics (age, sex, and race/ethnicity), location of cardiac arrest, initial cardiac arrest rhythm, and whether the arrest was witnessed. Additionally, information as to whether bystander cardiopulmonary resuscitation (CPR) or defibrillation with automated external defibrillator (AED) was administered prior to EMS arrival and cardiac arrest etiology (presumed cardiac, respiratory, drug overdose and other), is collected, as well as times to EMS arrival and duration of EMS treatment. The study was approved by Saint Luke's Mid America Heart Institute, which waived the requirement for informed consent because the analysis included only de-identified data (reference number, SLHS-20–054).

Study Population

We identified 457,621 patients with an OHCA in CARES between January 1, 2013 and December 31, 2019 (Fig. 1). We excluded 12,679 children with under 18 years of age. We then restricted our cohort to patients who were transported alive to the emergency department, excluding 150,842 patients who died before hospital arrival. As our focus was on patients with STEMI who underwent emergent coronary angiography (within 2 hours of hospital arrival), we excluded 208,310 patients without a STEMI, 71,229 with unavailable data on STEMI, 1,068 patients who were transferred to another facility, 10,493 patients who did not undergo early angiography, and 1 patient with missing information on witnessed status of their arrest. Our analytic cohort comprised 2,999 unique patients with STEMI and OHCA who underwent emergent coronary angiography.

Statistical Analysis

The primary outcome for the study was in-hospital mortality. We compared baseline characteristics between patients who died and survived to hospital discharge using chisquare tests for categorical variables and Student's *t*-tests for continuous variables when normally distributed or Wilcoxon's rank sum tests when not normally distributed.

To examine predictors of mortality, we constructed a multivariable logistic regression model with in-hospital mortality as the outcome and the following patient and cardiac arrest variables as candidates for model inclusion: age, sex, location of arrest at home, witnessed cardiac arrest, initial arrest rhythm (non-shockable vs. shockable), whether bystander CPR was performed, whether an AED was applied by a bystander, presumed arrest etiology (cardiac, respiratory, drug overdose, or other), whether ROSC was present at hospital arrival, and EMS resuscitation time on scene before transport to hospital. Race and ethnicity were not included in the model based on current recommendations for risk-adjustment models used for quality assessment.[12, 13]. As the test for non-linearity using restricted cubic splines for the continuous variable, resuscitation time on scene, was significant, this variable was categorized by 10-minute intervals to address non-linearity and to facilitate clinical interpretation.

To obtain a parsimonious model to illustrate the number of variables needed for better risk-adjustment in future benchmarking efforts, variable selection was performed according to Harrell's method.[14] Specifically, using the predicted values from the full model, we ranked all predictors by their R^2, and variables with the smallest contribution to the model were sequentially eliminated until removal resulted in more than a 5% loss in model prediction as compared with the initial full model (i.e., the reduced model and would retain 95% of the predictive power of the full model). Model discrimination and calibration were estimated using the area under the receiver-operating characteristic curve (AUC), or c-statistic, and observed versus predicted calibration plots for a given decile of predicted risk. Calibration of the observed versus predicted probabilities was also assessed over internal bootstrapped samples to evaluate risk of overfitting.[15]

We then applied the model coefficients from the parsimonious model to each patient to calculate their predicted probability of mortality. We examined the heterogeneity of predicted mortality risk in patients with OHCA and STEMI using descriptive statistics (median, inter-quartile range, and 10^{th} to 90^{th} percentiles).

In secondary analysis, we then derived a mortality risk score with the variables in the reduced model using the β coefficients, which were re-scaled and rounded to integers.[16] Performance and calibration of risk model were evaluated on a continuous scale.

In our study cohort, 31 (1.0%) patients had missing time on scene. Before development of the models, time was imputed with random forest imputation (missForest package version 1.4 in R).[17] All tests are 2-tailed, and an alpha level of 0.05 was considered statistically significant. All analyses were conducted using R statistical software version 4.1.0 (R Project for Statistical Computing).

RESULTS

Of 2,999 patients with OHCA and STEMI who survived to the emergency department and underwent emergent coronary angiography, 996 (33.2%) died during the hospitalization.

Mean age was 61.2 ±12.0, 693 (23.1%) patients were female and 1938 (64.6%) were of white race. Overall, 1829 (61.0%) had their OHCA at home, 489 (16.3%) had an unwitnessed cardiac arrest, 534 (17.8%) had an initial non-shockable rhythm, and 287 (9.6%) did not have sustained ROSC upon hospital arrival. The bystander CPR rate was 42.7%, and the rate of bystander use of an AED was 7.3%. A comparison of patients who survived and died is provided in Table 1. Patients who died were older, more often female and of non-white race, and were more likely to have an OHCA at home, an unwitnessed arrest, or initial non-shockable cardiac arrest rhythm; not be evaluated with an AED by a bystander; not have sustained ROSC at the time of hospital arrival; and have a longer resuscitation time on scene before EMS transport.

In the full multivariable model, we identified several variables associated with in-hospital mortality (Table 2; Supplemental Fig. 1A). These included higher age, female sex, arrest at home, unwitnessed arrest, lack of bystander deployment of an AED, initial non-shockable rhythm, no ROSC before hospital arrival, and longer resuscitation time on scene. The full model had excellent discrimination (c-statistic, 0.807) and calibration.

In the reduced model that retained 95% of the full model's predictive power (Table 2; Supplemental Fig. 1B), five key variables were retained to predict in-hospital mortality. These were older age (OR for every 10 years, 1.50 [95% CI: 1.39–1.63]), unwitnessed OHCA (OR, 2.51 [1.99–3.16]), non-shockable OHCA rhythm [OR, 5.66 [4.52–7.13]), no ROSC before hospital arrival (OR, 2.52 [1.88–3.36]), and longer resuscitation time (increased with each 10-minute interval). Model performance was similar with excellent discrimination (c-statistic, 0.804). Findings for both models were upheld in the internal bootstrap validation, with an optimism-corrected Area Under the Curve of 0.803 for the full model (Supplemental Fig. 2A) and 0.802 for the reduced model (Supplemental Fig. 2B).

Applying the model coefficients, we computed predicted mortality risk for each patient. Fig. 2 shows the distribution of predicted mortality risk in the study cohort. There was wide variability in the predicted mortality of patients in this cohort: median, 25.2%, inter-quartile range: 14.0% to 47.8%, 10^{th} to 90^{th} percentile: 8.2 % to 74.1%.

In secondary analysis, an integer risk score was developed from the 5 variables based on strength of association of their β coefficients in the reduced model. The risk score ranged from 0 to 8 points (Figure 3) and estimated that patients with STEMI and OHCA who underwent early angiography have an observed in-hospital mortality risk from 8.9% to 100%, with the odds of in-hospital mortality doubling for each additional point in the risk score (odds ratio, 2.04; 95% CI, 1.92–2.17; $p<0.001$; C-statistic, 0.775). The risk model calibration was excellent, as predicted vs. observed mortality were similar with a slope of near 1.000 (Supplemental Figures 1C). Findings for the model were also upheld in internal bootstrap validation, with an optimism of −0.0012 and optimism-corrected Area Under the Curve of 0.775, identical to the original c-statistic.

DISCUSSION

In a large, multi-site registry of OHCA patients, we developed a risk-adjustment model to predict mortality risk among patients presenting with OHCA and STEMI who underwent emergent coronary angiography. We found that approximately 1 in 3 patients died overall, with 5 key variables predicting hospital mortality—older age, unwitnessed arrest, non-shockable cardiac arrest rhythm, no ROSC before hospital arrival, and resuscitation time on scene. When the model was applied to patients in the study cohort, there was substantial heterogeneity in predicted mortality risk. Using the key predictors, we subsequently developed a mortality risk score (range: 0–8 points) that can stratify the risk of in-patient mortality for patients with STEMI and OHCA who undergo coronary angiography, from 8.9% in those with a score of 0 to 100% in those with the highest score of 8. Collectively, our findings underscore that a given patient with OHCA and STEMI has a wide range of mortality risk and use of this model can help inform current benchmarking efforts for coronary angiography.

OHCA remains a major public health challenge in the U.S. Although OHCA is present in only a fraction of patients who undergo coronary angiography, it is associated with a 10-fold higher mortality risk in STEMI patients.[1] Given its outsized impact on operator mortality rates, current models for national benchmarking of operator mortality rates for coronary angiography includes adjustment for OHCA.[7, 8] However, our findings suggest that adjustment for the mere presence of OHCA as a binary variable may be insufficient to account for patient case-mix given the heterogeneity in predicted mortality risk from our model. Our model suggests that inclusion of four additional variables in current data collection forms (since age is already collected) would provide more granular risk-adjustment for operator mortality rates.

Although OHCA risk models predicting mortality exist,[18–20] models to estimate mortality risk in patients with concurrent STEMI and undergoing emergent coronary angiography are lacking. Our model has the potential to inform clinicians or patients' family members of patients' overall in-hospital mortality risk for those undergoing emergent coronary angiography. However, our models and risk scores have not been prospectively or externally validated. Moreover, while some patients in our model have predicted mortality risks that are high (e.g., 90th percentile of 78.5%), our model does not estimate potential benefit from coronary revascularization even in the highest risk group, as all patients in our model underwent coronary angiography. Therefore, our model should not be used to make decisions regarding futility of treatment; rather, it could be used by clinicians to inform patients and families of their predicted mortality risk with emergent coronary angiography.

Limitations

This study should be considered in the context of the following potential limitations.

First, the CARES registry does not collect detailed clinical information on patients such as comorbidities and hemodynamic information that can affect mortality risk. Additionally, both STEMI and coronary angiography data are optional data elements and were only collected on approximately 75–80% of the cases. Nonetheless, it is unlikely that the predictors of in-hospital mortality for patients excluded due to missing information on coronary angiography differed substantially from those of our patient cohort. Second, we did not conduct a comparative effectiveness assessment of the benefits of emergent coronary angiography for patients with OHCA and STEMI. This is because our study objective was to build a model for risk adjustment for mortality using prehospital cardiac arrest variables in patients with OHCA and STEMI undergoing emergent coronary angiography. Third, our models may require prospective and even external validation in future studies. Nonetheless, we believe our main objective—to highlight the incomplete adjustment of the heterogeneity of OHCA patient risk in current benchmarking efforts—is supported by this study's findings. Finally, CARES is a voluntary registry for OHCA, our findings may not be generalizable to non-participating sites. Nonetheless, we have no reason to expect model predictors to differ for OHCAs in non-participating sites.

CONCLUSIONS

In a large national registry, we identified 5 key predictors for mortality in patients with STEMI and OHCA and found wide variability in predicted mortality risk. Our findings suggest that current national benchmarking efforts for coronary angiography, which simply adjusts for the presence of OHCA, may not adequately capture patient case-mix severity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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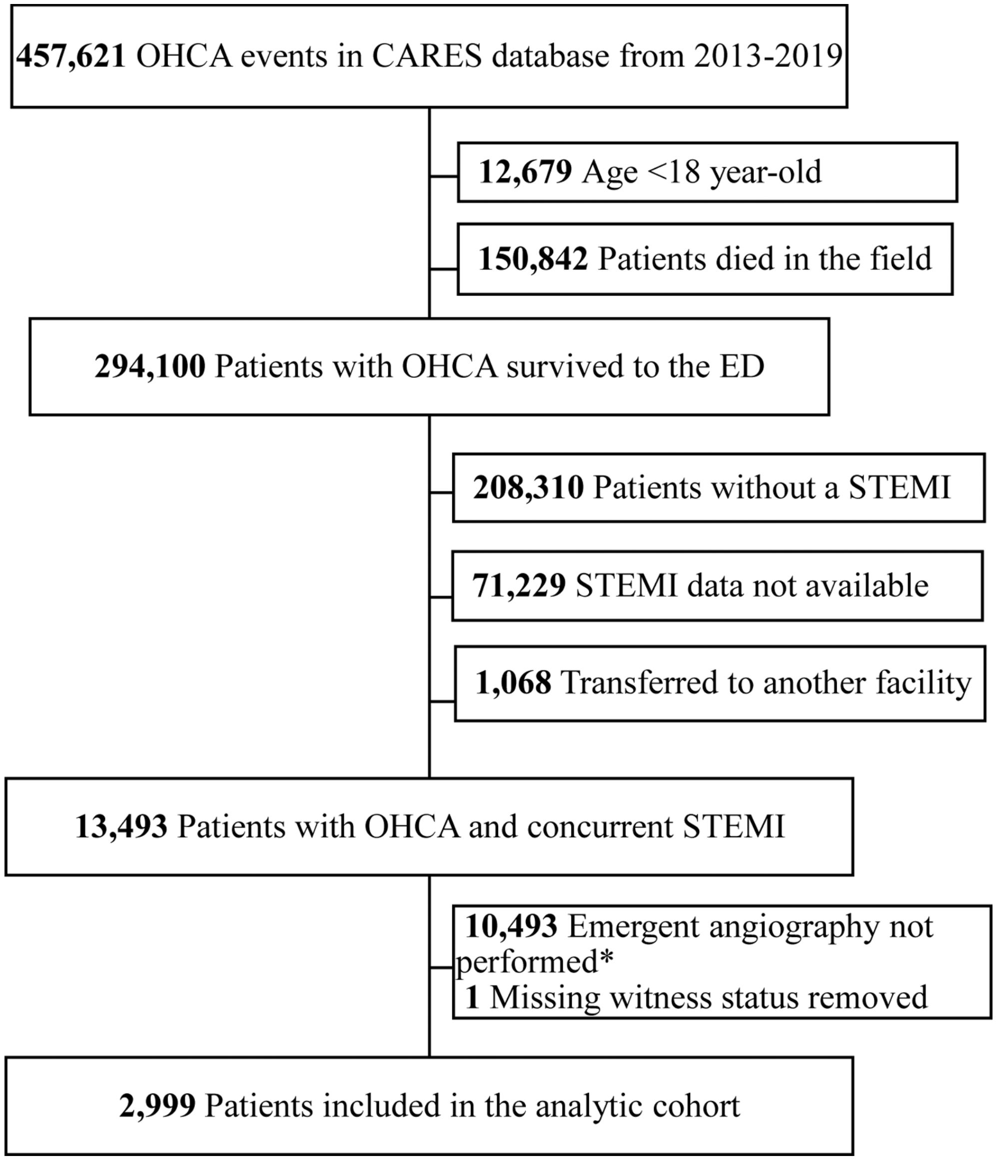

Fig. 1: Study Cohort

*Emergent angiography is defined as emergent coronary angiography performed within 2 hours of hospital arrival. CAG indicates coronary artery angiography; CARES, Cardiac Arrest Registry to Enhance Survival; CPR, cardiopulmonary resuscitation; ED, emergency department; OHCA, out-of-hospital cardiac arrest; STEMI, ST-Elevation Myocardial Infarction.

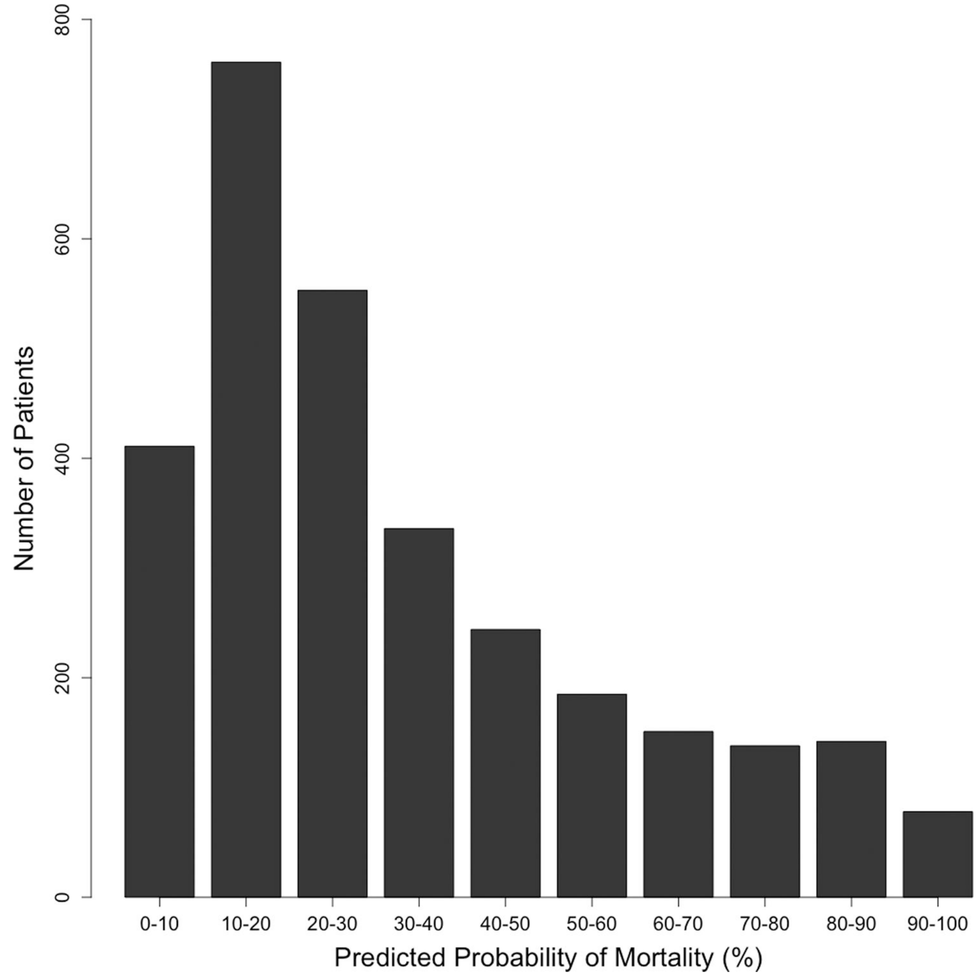

Fig. 2: Distribution of Predicted Mortality Risk in Patients with STEMI and OHCA

Patients varied widely in their predicted mortality risk based on their patient and arrest factors. The proportion of those who actually died in each risk decile is also shown. OHCA indicates out-of-hospital cardiac arrest; STEMI, ST-Elevation Myocardial Infarction.

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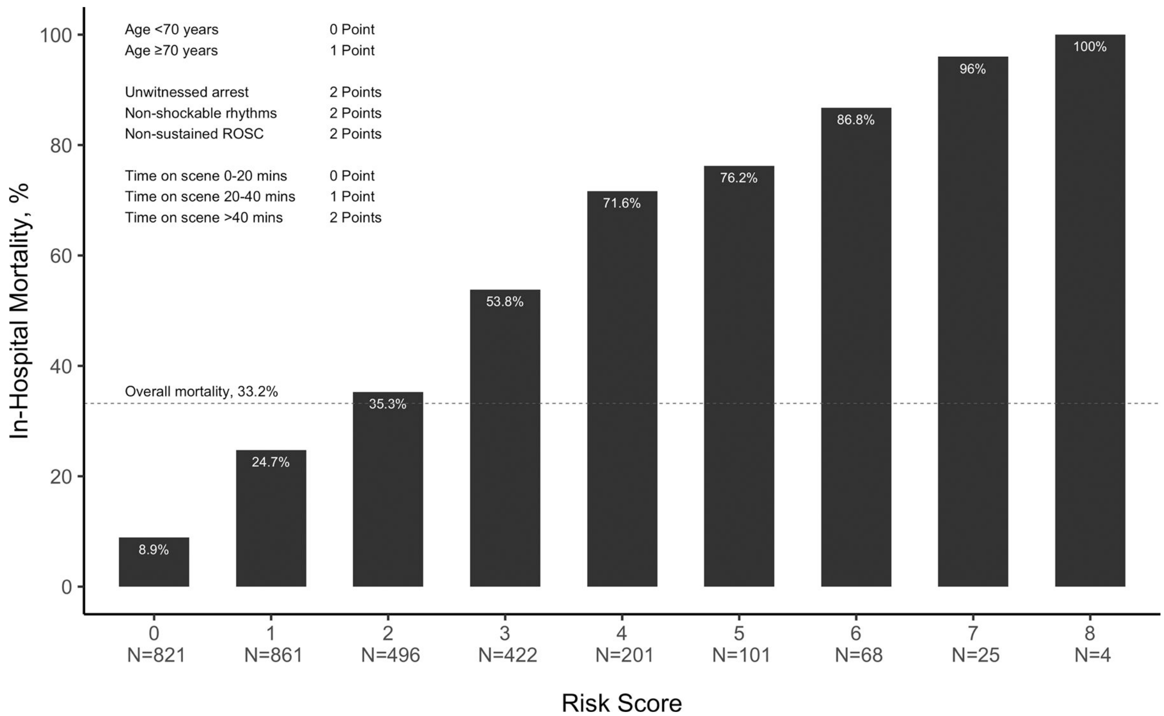

Fig. 3: Observed In-Hospital Mortality Rate by Risk Score

ROSC indicates return of spontaneous circulation.

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Table 1:

Baseline Characteristics of Study Cohort, Stratified by Mortality Status

	Total (N=2999)	Died (N=996)	Survived (N=2003)	*p*-value
Age, year	61.2 (12.0)	64.8 (12.2)	59.4 (11.4)	<0.001
Female	693 (23.1)	290 (29.1)	403 (20.1)	<0.001
Race/ethnicity				0.018
White	1938 (64.6)	622 (62.4)	1316 (65.7)	
Black	280 (9.3)	117 (11.7)	163 (8.1)	
Hispanic	114 (3.8)	41 (4.1)	73 (3.6)	
Asian	49 (1.6)	19 (1.9)	30 (1.5)	
Other/unknown	618 (20.6)	197 (19.8)	421 (21.0)	
Arrest at home	1829 (61.0)	699 (70.2)	1130 (56.4)	<0.001
Unwitnessed arrest	489 (16.3)	264 (26.5)	225 (11.2)	<0.001
Bystander CPR	1280 (42.7)	434 (43.6)	846 (42.2)	0.510
Bystander AED applied	220 (7.3)	45 (4.5)	175 (8.7)	<0.001
Non-shockable rhythms (non-PVT/VF)	534 (17.8)	381 (38.3)	153 (7.6)	<0.001
Non-sustained ROSC >20 minutes	287 (9.6)	153 (15.4)	134 (6.7)	<0.001
Presumed arrest etiology				<0.001
Presumed cardiac	2942 (98.1)	961 (96.5)	1981 (98.9)	
Respiratory/asphyxia	36 (1.2)	22 (2.2)	14 (0.7)	
Drug overdose	4 (0.1)	3 (0.3)	1 (0.0)	
Other	17 (0.6)	10 (1.0)	7 (0.3)	
Time to arrival, minute	7.2 [5.2, 9.8]	7.1 [5.2, 9.8]	7.2 [5.2, 9.9]	0.980
Time on scene, minute	20.9 [15.0, 28.0]	25.5 [19.3, 33.6]	18.8 [13.4, 25.0]	<0.001
Transport time, minute	11.4 [7.6, 17.7]	11.0 [7.0, 16.3]	11.7 [7.7, 18.4]	0.004
Total response time, minute	42.0 [33.3, 53.0]	46.0 [37.5, 58.0]	40.1 [32.0, 50.4]	<0.001

Values are mean (standard deviation), median [25^{th} – 75^{th} interquartile range], or n (%).

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; PVT, pulseless ventricular tachycardia, ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

Table 2:

Multivariable Logistic Regression Model for In-hospital Mortality

Characteristic	Full Model			Reduced Model		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age, per 10-year increase	1.49	1.38–1.62	<0.001	1.50	1.39–1.63	<0.001
Female	1.32	1.07–1.63	0.01	*removed*		
Arrest at home/residence	1.14	0.94–1.40	0.20			
Unwitnessed arrest	2.48	1.96–3.13	<0.001	2.51	1.99–3.16	<0.001
Bystander CPR	1.21	1.00–1.47	0.05	*removed*		
Bystander AED applied	0.61	0.40–0.92	0.02			
Non-shockable rhythms (Asytole and PEA)	5.62	4.45–7.13	<0.001	5.66	4.52–7.13	<0.001
Non-sustained ROSC >20 minutes	2.50	1.87–3.35	<0.001	2.52	1.88–3.36	<0.001
Presumed arrest etiology			0.60	*removed*		
Presumed Cardiac	*ref*	—				
Respiratory/Asphyxia	0.80	0.37–1.80				
Drug Overdose	4.28	0.31–129				
Other	1.40	0.45–4.59				
Resuscitation Time on scene			<0.001			<0.001
0 to ≤10 minutes	*ref*	—		*ref*	—	
10 to ≤20 minutes	2.64	1.68–4.32		2.75	1.75–4.47	
20 to ≤30 minutes	5.49	3.50–8.96		5.91	3.79–9.58	
30 to ≤40 minutes	9.63	5.91–16.2		10.5	6.52–17.6	
40 to ≤50 minutes	15.0	8.27–27.9		16.1	8.95–29.8	
>60 minutes	18.3	9.25–37.3		21.0	10.7–42.5	
Model *c*-statistic	0.807			0.804		

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation