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Clinical paper

The cardiac arrest survival score: A predictive algorithm for in-hospital mortality after out-of-hospital cardiac arrest

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Abstract

Background: Out-of-hospital cardiac arrest (OHCA) is associated with high mortality. Current methods for predicting mortality post-arrest require data unavailable at the time of initial medical contact. We created and validated a risk prediction model for patients experiencing OHCA who achieved return of spontaneous circulation (ROSC) which relies only on objective information routinely obtained at first medical contact.

Methods: We performed a retrospective evaluation of 14,892 OHCA patients in a large metropolitan cardiac arrest registry, of which 3952 patients had usable data. This population was divided into a derivation cohort (n = 2,635) and a verification cohort (n = 1,317) in a 2:1 ratio. Backward stepwise logistic regression was used to identify baseline factors independently associated with death after sustained ROSC in the derivation cohort. The cardiac arrest survival score (CASS) was created from the model and its association with in-hospital mortality was examined in both the derivation and verification cohorts.

Results: Baseline characteristics of the derivation and verification cohorts were not different. The final CASS model included age >75 years (odds ratio [OR] = 1.61, confidence interval [CI][1.30–1.99], $p < 0.001$), unwitnessed arrest (OR = 1.95, CI[1.58–2.40], $p < 0.001$), home arrest (OR = 1.28, CI[1.07–1.53], $p = 0.008$), absence of bystander CPR (OR = 1.35, CI[1.12–1.64], $p = 0.003$), and non-shockable initial rhythm (OR = 3.81, CI[3.19–4.56], $p < 0.001$). The area under the curve for the model derivation and model verification cohorts were 0.7172 and 0.7081, respectively.

Conclusion: CASS accurately predicts mortality in OHCA patients. The model uses only binary, objective clinical data routinely obtained at first medical contact. Early risk stratification may allow identification of more patients in whom timely and aggressive invasive management may improve outcomes.

Keywords: Cardiac arrest, Risk stratification

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Introduction

Out-of-hospital cardiac arrest (OHCA) affects an estimated 350,000 patients in the United States annually and is associated with high mortality.[1] Despite advances in resuscitation and post-arrest care, survival rates remain dismal, estimated at less than 10%.[2–6] Recent studies, however, have suggested that in certain carefully selected patient subsets, aggressive invasive management may improve outcomes. A recent analysis of Extracorporeal Life Support Organization (ELSO) registry data reported a survival rate of 27.6% in refractory OHCA patients who underwent extracorporeal membrane oxygenation (ECMO).[7] Similarly, Yannopoulus et al. reported a survival rate of 45% in appropriately selected patients with refractory OHCA secondary to ventricular fibrillation who underwent immediate ECMO plus coronary revascularization.[8] However, outside of select scenarios where consensus for aggressive interventions exists, there remains significant debate regarding optimal treatment pathways and especially how to identify those patients who will truly benefit from aggressive invasive therapies after experiencing OHCA.[9]

Delineation of factors that may potentially impact outcomes in the setting of OHCA has been the subject of on-going investigations. Previous literature has suggested multiple predictors of poor outcomes, including older age, unwitnessed arrest, lack of bystander cardiopulmonary resuscitation (CPR), non-shockable initial rhythm (pulseless electrical activity or asystole), prolonged time to return of spontaneous circulation (ROSC), evidence of refractory systemic hypoperfusion and circulatory failure, medical history of end-stage renal disease, and cardiac arrest due to non-cardiac etiologies.[10–20] In an advisory article published by the Interventional Scientific Council of the American College of Cardiology, a proposed clinical algorithm was developed with a focus on the above mentioned predictors of poor outcome, advising that patients with multiple unfavorable resuscitation features are less likely to benefit from aggressive invasive management.[9] However, no study to date has evaluated the relative weights of these variables and there remains a need for a validated method of early prediction and risk stratification to help guide management of patients after OHCA. The goal of this investigation was to derive and validate a simple risk assessment model that incorporates only binary, objective information available at first medical contact.

Methods

Data source

The Houston Fire Department Registry (HFDR) contains information regarding encounters with OHCA patients by emergency medical services in the Houston region. Two databases, consisting of patient data between 2007 to 2012 and 2013 to 2015, make up the registry. Research personnel prospectively collected patient-level data from consecutive OHCA encounters during these time periods.

Study design and population

Using the HFDR, we performed a retrospective analysis of OHCAs, defined as arrests occurring prior to arrival to any hospital, between January 2007 and December 2015. Patients included in the analysis were those in whom sustained ROSC was achieved after OHCA, regardless of presumed cause. The exclusion criteria were age <18 years of age and absence of data regarding patient outcome at time of hospital discharge. The primary outcome variable was in-hospital mortality. The Institutional Review Board (IRB) of the University of Texas Health Science Center Houston approved this study.

Statistical analysis and creation of the cardiac arrest survival score model

Individual patients were randomly assigned to either the model derivation cohort or model verification cohort in a 2:1 ratio. Baseline variables were compared between the model derivation and model verification cohorts. We used the Student's t-test or Wilcoxon rank-

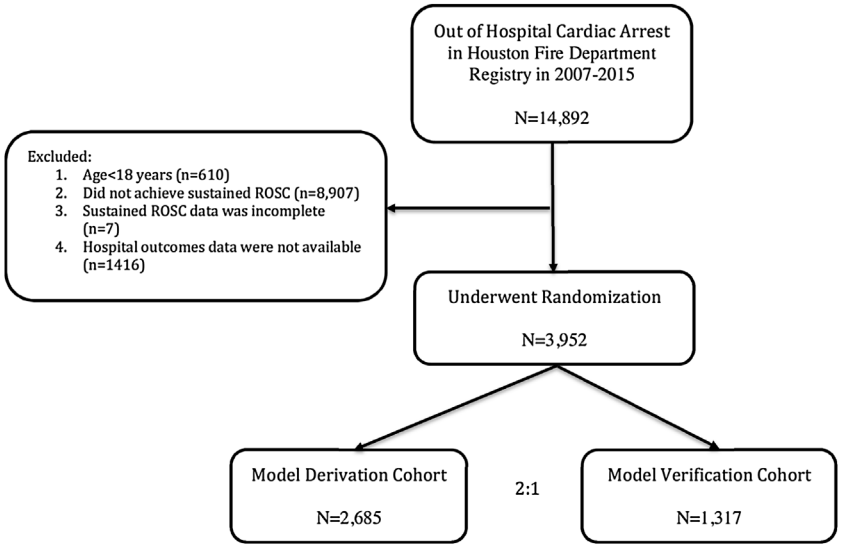

Fig. 1 – Study design.
Abbreviation: ROSC = Return of Spontaneous Circulation.

sum test for continuous variables and Fisher exact test for all dichotomous variables. Univariate analyses examining various parameters and their associations with in-hospital mortality in the model derivation group were performed. The variables studied included patient demographics such as age, gender, and race as well as information that was readily available upon initial medical contact such as the presence of a witness to the arrest, location of arrest (i.e. at home versus in a public place), the presence or absence of bystander CPR (defined as CPR performed by any persons prior to initial medical contact), non-shockable rhythm upon initial medical contact (i.e. pulseless electrical activity or asystole), and application of an automated external defibrillator (AED) regardless of whether a shock was or was not delivered. Characteristics with $p < 0.2$ in the univariate logistic regression analysis were subsequently entered into a backward stepwise logistic regression analysis with bootstrap for 1000 replications and an exit criterion on $p > 0.2$ to determine their associations with patient survival to hospital discharge. Predictor variables which remained within the stepwise logistic regression model were assigned weights to facilitate the formation of the prognostic model. The Hosmer–Lemeshow test was performed to determine the goodness of fit of the model. A p-value of 0.05 or more indicates that there is no significant difference between observed and expected count of outcomes across all risk levels. Weighted values were obtained by multiplying the odds ratios for mortality associated with each of the variables by two and rounding to the nearest 0.5. The sum of the weighted values yields the cardiac arrest survival score (CASS). CASS was calculated for all patients and the discrimination and calibration of the score were assessed in the model derivation and model verification cohorts by calculating the area under the curve (AUC) and the Hosmer–Lemeshow test. The AUC and the estimated probabilities of in-hospital death based on the score for the verification cohort were compared with those obtained from the derivation cohort. The CASS values were stratified into 4 groups ($<=5$, 5–10, 10–15 and >15) with comparison of observed and expected outcomes in each group. All statistical analyses were performed using the STATA-14 software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX. StataCorp, LP).

Results

Patient demographics and outcomes

Between January 2007 and December 2015, data from 14,892 patients who experienced OHCA were entered into the HFDR databases. 610 patients were under 18 years of age, while 8907 patients did not achieve ROSC despite resuscitation efforts and 7 did not have resuscitation outcomes recorded. Out of the 5368 patients who had documented sustained ROSC, 1416 patients had missing data regarding outcomes at time of hospital discharge. There were 3952 patient records (73.6% of patients in whom ROSC was achieved) that underwent assignment into the model derivation and model verification cohorts. The study design flow diagram is shown in Fig. 1.

Mean patient age for each of the two cohorts was 63.33 ± 0.30 years and 62.96 ± 0.43 years, respectively ($p = 0.472$). The model derivation cohort consisted of 33% Caucasians, whereas the model verification cohort consisted of 35% ($p = 0.138$). The male-to-female ratios were approximately 1.6:1 in both cohorts ($p = 0.575$). There were no significant differences in baseline patient demographics between the two cohorts. The demographic data are shown in Table 1. There was also no significant difference in the primary outcome of in-hospital mortality between the derivation and verification cohorts (66.19% vs. 67.69%, $p = 0.267$) (Table 1).

Univariate analysis

Univariate analysis in the model derivation cohort revealed seven variables which were potentially associated with patient mortality prior to hospital discharge. These variables included older age (greater than 75 years), male gender, unwitnessed arrest, arrest at home, absence of bystander CPR, non-shockable initial rhythm, and AED use. Except for AED use ($p = 0.042$), all other identified variables had p-values less than 0.005. AED use was defined as application of the AED regardless of whether a shock was delivered, potentially

Table 1 – Demographic characteristics of model derivation and model verification cohorts.

	Total N = 3952	Model derivation cohort, n (%) N = 2685	Model verification cohort, n (%) N = 1317	p-Value*
Age, mean ± SD	63.21 ± 15.44	63.33 ± 0.30	62.96 ± 0.43	0.4720
Gender, male	2298 (58.15%)	1524 (57.84%)	774 (58.77%)	0.575
Race				0.746
Caucasian	1333 (33.73%)	868 (32.94%)	465 (35.31%)	
Black	1666 (42.16%)	1130 (42.88%)	536 (40.7%)	
Hispanic	767 (19.41%)	515 (19.54%)	252 (19.13%)	
Asian	124 (3.14%)	81 (3.07%)	43 (3.26%)	
Other	18 (0.46%)	12 (0.46%)	6 (0.46%)	
Unknown	44 (1.11%)	29 (1.1%)	15 (1.14%)	
Home Arrest	2639 (66.78%)	1764 (66.94%)	875 (66.44%)	0.388
Unwitnessed Arrest	1291 (32.67%)	841 (31.92%)	450 (34.17%)	0.083
Absence of Bystander CPR	2366 (59.9%)	1585 (60.2%)	781 (59.3%)	0.306
Non-shockable Initial Rhythm	2740 (69.33%)	1846 (70.06%)	894 (67.88%)	0.087
AED used	733 (18.55%)	474 (17.99%)	259 (19.67%)	0.208
In-hospital-death	2639 (66.78%)	1774 (66.19%)	895 (67.69%)	0.267

Abbreviations: CPR, cardiopulmonary resuscitation; AED, automated external defibrillator.
* p-values were derived using t-test for continuous age and Fisher exact test for all other variables.

Table 2 – Univariate analysis in the model derivation cohort.

	Odds ratio (95% CI)	*p*-value
Age greater than 75	1.87 (1.53–2.28)	<0.001
Caucasian race	1.01 (0.97–1.04)	0.715
Male gender	0.80 (0.68–0.94)	0.008
Unwitnessed arrest	2.46 (2.03–2.97)	<0.001
Arrest at home	1.62 (1.37–1.92)	<0.001
Absence of bystander CPR	1.68 (1.42–1.99)	<0.001
Non-shockable initial rhythm	4.37 (3.66–5.22)	<0.001
AED used	1.19 (1.00–1.41)	0.042

explaining the lack of a relationship with patient outcome. Results of the univariate regression analysis are shown in Table 2.

Multivariable analysis and cardiac arrest survival score

Seven significant variables from the univariate analysis were included in a stepwise logistic regression analysis and five of them remained in the final model. These variables included age >75 years (odds ratio [OR] = 1.61, confidence interval [CI][1.30–1.99], $p < 0.001$), unwitnessed arrest (OR = 1.95, CI [1.58–2.40], $p < 0.001$), home arrest (OR = 1.28, CI[1.07–1.53], $p = 0.008$), absence of bystander CPR (OR = 1.35, CI[1.12–1.64], $p = 0.003$), and non-shockable initial rhythm (OR = 3.81, CI[3.19–4.56], $p < 0.001$). The model showed adequate calibration and discrimination with an area under the curve (AUC) = 0.72 (Hosmer–Lemeshow test $p = 0.36$). To simplify the prediction model, each variable was assigned a weight as previously described in the Methods section (Table 3). The cardiac arrest survival score (CASS) was subsequently calculated for each patient and used to predictin-hospital mortality.

Model verification

The CASS value was calculated for all patients within the model derivation and model verification cohorts. Results were compared with patient outcomes, and receiver- operating characteristic (ROC) curves for both cohorts were generated. The observed versus predicted patient outcomes in each stratum based on the CASS value are shown in Fig. 2A and 2B for the model derivation and verification cohorts, respectively. The area under the ROC curve for the CASS prediction model in the model verification cohort was 0.7081. The goodness-of-fit test revealed a p-value of 0.3356. The area under the ROC curve for the CASS prediction model in the derivation cohort was 0.7172. The goodness-of-fit test had a p-value of 0.3599. Fig. 3A displays the ROC curves for both the model derivation and model verification cohorts. Survival to hospital discharge by CASS is plotted in Fig. 3B. Increasing CASS was inversely associated with probability of survival to hospital discharge. In other words, lower CASS corresponds to greater chance of survival and higher CASS corresponds to greater chance of death.

Discussion

OHCA remains a complex problem requiring coordination of a multitude of resources to improve survival and outcomes. Improving outcomes requires building a chain of survival that begins with bystander CPR, the use of automated external defibrillators (AEDs), and targeted temperature management.[21–24] Next steps include rapid triage to a capable receiving hospital with the goal of appropriately identifying patients who may benefit from aggressive invasive therapies. Recent research has documented that in appropriately selected patients, a rapid and aggressive invasive approach combining hemodynamic support with coronary revascularization can provide significant improvements in survival.[7,8] Prompt and appropriate patient selection therefore becomes an important part of the algorithm in cardiac arrest management. In this study, we present a simple risk assessment model titled the cardiac arrest survival score (CASS) which quickly and accurately estimates the risk of in-hospital mortality among patient with ROSC after OHCA. The most important aspect of the clinical variables in this model is the objective, binary nature of the information and rapid availability at first medical contact.

There have been several prior published models attempting to predict the risk for adverse outcomes after OHCA in the point-of-care clinical setting to guide clinical management. Bascom et al. described a method which stratified risk for circulatory-etiology death based on (1) known coronary artery disease prior to the inciting event, (2) initial heart rhythm, (3) left ventricular ejection fraction less than 30% by echocardiography within 12 h from time of admission, (4) shock at initial presentation, and (5) ischemic time greater than 25 min.[25] Maupain et al. devised a prognostic model for poor neurological outcome (defined as Cerebral Performance Category 3, 4, or 5 at hospital discharge) using similar indicators such as 1) time from collapse to basic life support, 2) time from basic life support to ROSC, and 3) initial heart rhythm in addition to other factors such as age, location of OHCA, epinephrine dose, and arterial pH.[26]

Although parameters used in both models have been validated by previous studies to have prognostic value, the information required for the appropriate use of the models may preclude their use for risk stratification at a sufficiently early time point to guide clinical decision making and management. Furthermore, reported ischemic times and resuscitation delays are often not available or unreliable as events may be unwitnessed and errors in time estimation frequently occur. As the probability for cardiovascular mortality and poor neurologic

Table 3 – Multivariable model in the derivation cohort and variable weight assignments.

	Odds ratio (95% CI)	*p*-value	Weighted value
Age greater than 75	1.61 (1.30–1.99)	<0.001	3.0
Unwitnessed Arrest	1.95 (1.58–2.40)	<0.001	4.0
Arrest at Home	1.28 (1.07–1.53)	0.008	2.5
Absence of Bystander CPR	1.35 (1.11–1.64)	0.003	2.5
Non-Shockable Initial Rhythm	3.81 (3.19–4.56)	<0.001	8

Abbreviations: CPR, cardiopulmonary resuscitation; AED, automated external defibrillator.

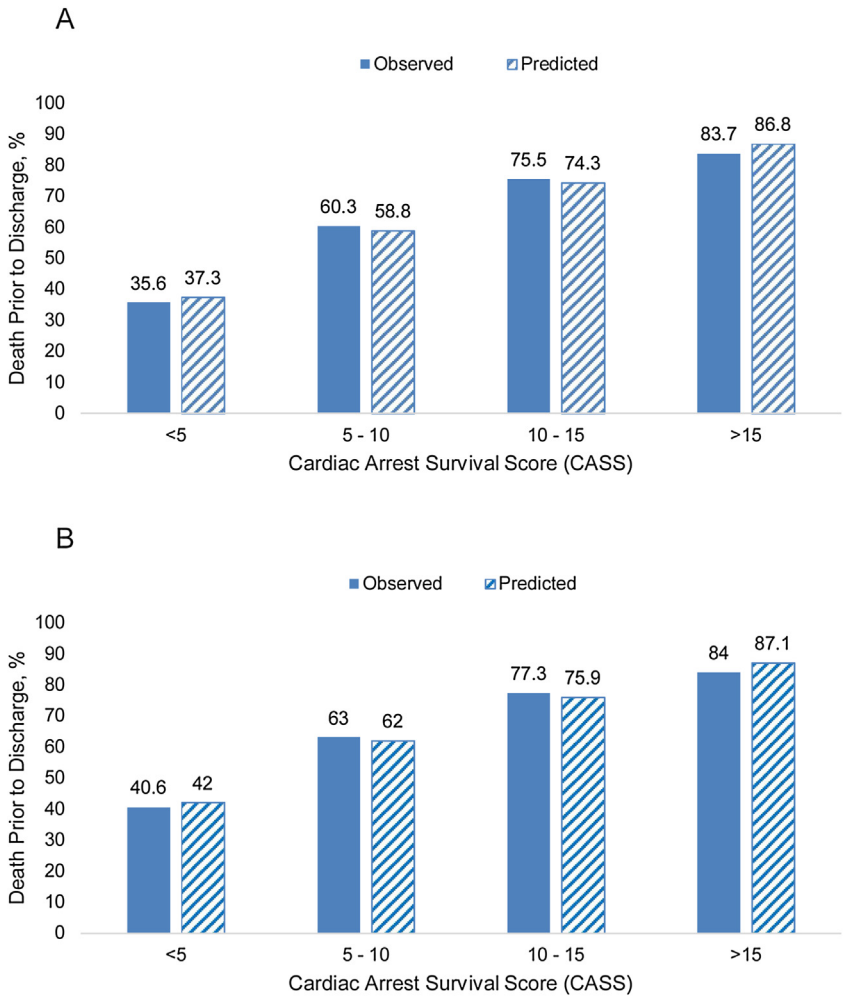

Fig. 2 – Observed versus predicted outcomes in CASS stratums.
Note: A. Comparison of observed versus predicted outcomes in model derivation cohort; B. Comparison of observed versus predicted outcomes in model verification cohort. Abbreviation: CASS = cardiac arrest survival score.

recovery increases exponentially with prolonged durations, errors in estimating ischemic time may result in significant variability in predicted outcomes. The medical history of patients are also frequently not known to medical providers, particularly in the early phases of resuscitation management when interventions are likely to provide the most benefit. The requirement for additional testing such as echocardiography may cause considerable delays in decision making in the real-world clinical setting, particularly when special expertise is necessary for its performance and interpretation. In fact, in one study which utilized estimated ischemic time or information acquired after initial medical contact, a significant number of patients were excluded from the statistical analysis as such data were not available.[25]

In our study, we present a prognostic model for survival after OHCA which relies only on binary, objective information routinely obtained at first medical contact. Although the algorithm proposed by Rab et al. provides a general guideline to assist decision makers in risk stratifying OHCA patients,[9] CASS aims to focus this algorithm and streamline it in such a way as to allow for rapid transmission of relevant information while taking into account the relative weights of contributing variables. In this retrospective analysis of 3952 OHCA patients who had successfully achieved ROSC, the observed rate of survival to discharge in patients achieving ROSC is 33.2 percent (9.1 percent of the entire adult OHCA cohort), consistent with previously published reports. Each of the variables included in CASS have been previously validated to have prognostic value. Furthermore, the relative weighting of each variable is consistent with previously published studies.[13,15,19,27–30]

Risk prediction models have obvious utility in research, where appropriate categorization of patients facilitates the identification of therapies targeted toward specific patient subsets, thereby improving patient management. In high-risk populations such as OHCA patients, the ability to stratify risk early in the clinical course may have other important implications. Current methods for reporting key operator and hospital metrics as well as rewarding systems for high performance in such measures provide tremendous disincentives against early invasive interventions and promote risk-avoidant behavior in this high-risk cohort.[9,31–34] Some may also argue against invasive interventions when efforts are perceived as futile and the associated cost of care is high. Defining medical futility is a complex subject that requires consideration of both quantitative futility, where the statistical chance that a particular intervention will alter the outcome is low, and qualitative futility, where the perceived benefit of an intervention may be poor.[35,36] A consensus on a method for risk

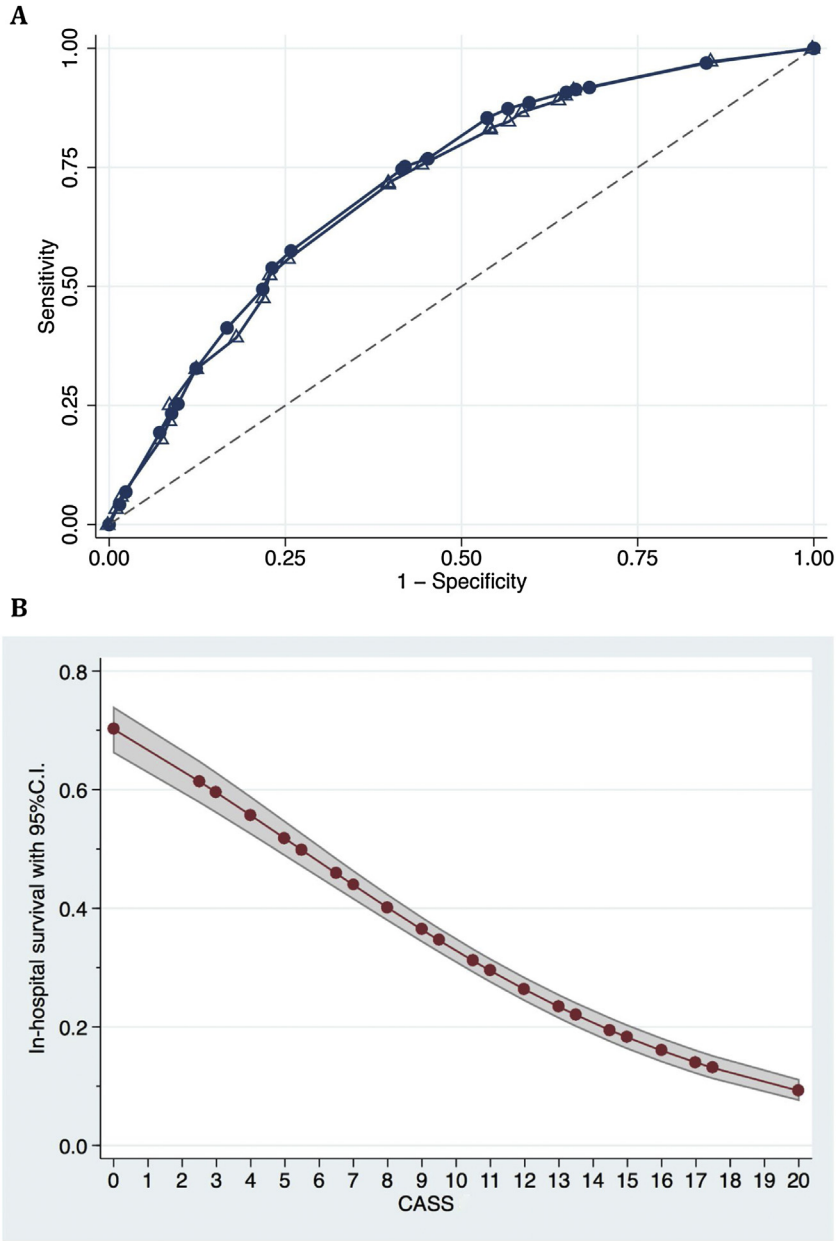

Fig. 3 – Validation of the predictability of CASS.
Note: A: Comparison of ROC curves for CASS model in derivation and verification cohorts. Dot: derivation cohort; Triangle: verification cohort; B: Prediction of CASS in survival to hospital discharge. Abbreviation: CASS = cardiac arrest survival score.

stratification in high risk populations such as OHCA patients allows for proper risk adjustment when reporting operator metrics and alleviates its effects on clinical management decisions. Although issues of qualitative futility are more subjective and require individualized discussion in particular clinical circumstances, the data presented here may provide some guidance with respect to quantitative futility and appropriate resource allocation.

There are several limitations to our study. First, as a retrospective analysis, our study may be subject to recording deficiencies and inaccuracies. In particular, missing information during time of resuscitation as well as at time of discharge led to the elimination of a sizable group of patients from the study, thereby decreasing the validity and applicability of our findings. Second, using clinical information at the initial point of contact likely presents only a static snapshot in a complex series of events and may not reflect the clinical evolution throughout the course of hospitalization. The utility of our prognostication system in guiding clinical management decisions is likely limited to the critical initial stages. Incorporation of additional variables such as pH, lactate, renal and liver function tests would likely improve the ability to estimate ischemic severity at the time of arrival to the receiving hospital. Similarly, additional testing such as imaging and EEG may increase the performance of the prediction model further into the hospital course. It is, however, our contention that one should not wait until this late in the clinical pathway to start making

clinical decisions in this vulnerable population. Third, the ability to further categorize mortality into cardiovascular etiology of death (CED) and neurological etiology of death (NED) may be valuable in identifying with greater accuracy patients who may benefit from early aggressive interventions.[25] However, the vast majority of patients that achieve cardiovascular survival also achieve reasonable neurologic survival with cerebral performance category 1 or 2. Thus, the ability to stratify patients according to their probability for cardiovascular survival remains of primary value in early clinical decision making. Additionally, although some studies suggest early neurologic prognostication based on specific EEG findings may be feasible, current guidelines recommend against early neurologic prognostication given the lack of reliable, validated methods.[37] The American Heart Association also advocates against the use of early neurologic prognostication in deciding whether to pursue urgent cardiac catheterization for similar reasons.[38] Fourth, inclusion of information regarding prehospital and hospital management such as rates of targeted temperature management and early coronary angiography would bring greater transparency to our statistical analysis and increase the generalizability of our model. A prospective study involving a data registry which includes such information would be an essential next step in the validation of our model. Finally, data generated in the study are not intended to provide any numerical thresholds which supplant clinical judgment. As with other risk assessment models, CASS should be used only to augment but not to supplant clinical judgement and thoughtful decision making.

Conclusion

CASS is a simple, easy-to-use risk-stratification model, which accurately predicts in-hospital mortality in OHCA patients who have achieved ROSC. The model is designed to augment medical decision making for early interventions by using only objective clinical data, which are routinely obtained at first medical contact. This study provides retrospective validation of the predictive ability of the instrument. Early risk stratification may allow identification of more patients in whom aggressive and timely invasive management approaches may improve outcomes. Further work is needed to improve the utility of CASS, particularly prospective validation of the model.

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None.

Conflicts of interest

Prakash Balan serves as a consultant for Osprey Medical, Abiomed, & Chiesi.

None of the other authors report any disclosures relevant to the subject of this study.

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