

Clinical Prediction Rule for Patient Outcome after In-Hospital CPR: A New Model, Using Characteristics Present at Hospital Admission, to Identify Patients Unlikely to Benefit from CPR after In-Hospital Cardiac Arrest



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BACKGROUND: Physicians and patients frequently overestimate likelihood of survival after in-hospital cardiopulmonary resuscitation. Discussions and decisions around resuscitation after in-hospital cardiopulmonary arrest often take place without adequate or accurate information.

METHODS: We conducted a retrospective chart review of 470 instances of resuscitation after in-hospital cardiopulmonary arrest. Individuals were randomly assigned to a derivation cohort and a validation cohort. Logistic Regression and Linear Discriminant Analysis were used to perform multivariate analysis of the data. The resultant best performing rule was converted to a weighted integer tool, and thresholds of survival and nonsurvival were determined with an attempt to optimize sensitivity and specificity for survival.

RESULTS: A 10-feature rule, using thresholds for survival and nonsurvival, was created; the sensitivity of the rule on the validation cohort was 42.7% and specificity was 82.4%. In the Dartmouth Score (DS), the features of age (greater than 70 years of age), history of cancer, previous cardiovascular accident, and presence of coma, hypotension, abnormal PaO₂, and abnormal bicarbonate were identified as the best predictors of nonsurvival. Angina, dementia, and chronic respiratory insufficiency were selected as protective features.

CONCLUSIONS: Utilizing information easily obtainable on admission, our clinical prediction tool, the DS, provides physicians individualized information about their patients' probability of survival after in-hospital cardiopulmonary arrest. The DS may become a useful addition to medical expertise and clinical judgment in evaluating and communicating an individual's probability of survival after in-hospital cardiopulmonary arrest after it is validated by other cohorts.

KEYWORDS: cardiopulmonary resuscitation, in-hospital cardiac arrest, code status

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Introduction

Cardiopulmonary resuscitation (CPR) was introduced in 1960 to revive victims of acute insult in otherwise good physiological condition.¹ In the past 50 years, CPR evolved from unorganized actions by untrained staff to synchronized teamwork and has become a fundamental part of medical care for all hospitalized patients in cardiac arrest. Despite these changes, survival from CPR to hospital discharge remains low. In 2008 and 2009, the reported survival from in-hospital cardiac arrest to hospital discharge varied between 15.4%² and 22.3%.³

In the 1980s, responding to demands for patient autonomy, many hospitals began instituting *Do Not Resuscitate* (DNR) policies, allowing patients or their families to determine that no resuscitation be attempted in the event of a cardiac arrest. However, less than 25% of seriously ill patients discuss preferences for resuscitation with

their physicians.^{4–6} Less than 50% of inpatients who prefer not to receive CPR have DNR orders written.^{7–9} A known obstacle to the conversation is physician reluctance to discuss the issue.^{10,11}

Despite being asked to predict the future frequently by patients, most physicians avoid prognostication, largely because they believe they do not have sufficient information to estimate outcomes.¹² When physicians do engage in this conversation, they overestimate the likelihood of survival to hospital discharge after in-hospital CPR by as much as 300%, and they predict a success rate that is twice that actually observed.¹³ This optimism strongly influences the choices of their patients. Accurate information about the probability of survival to discharge after CPR significantly alters patients' DNR preferences^{14,15} and might be helpful to patients and their physicians in deciding whether to forego this intervention.



A tool, or clinical prediction rule, utilizing admission data to estimate an individual's risk of not surviving CPR, could empower physicians to prognosticate more accurately, increase frequency of code status discussions, and thereby promote patient autonomy. In the late 1980s and early 1990s, three morbidity scores, Pre-Arrest Morbidity score (PAM),¹⁶ Prognosis after Resuscitation score (PAR),¹⁷ and Modified PAM Index (MPI),¹⁸ attempted to predict survival after resuscitation based on univariate meta-analysis (PAR), literature review (MPI), or stepwise logistic regression (PAM). However, changes in CPR algorithms, a changing and ageing population, and advances in medical science in the past 20 years have led to a need to update these tools. In addition, advances in the use of computational sciences allow increasingly sophisticated multivariate and multidimensional analysis of data.

Since the creation of the *In-Hospital Utstein Style Template*¹⁹ for summarizing data elements desirable for documenting in-hospital cardiac arrest and reporting outcome data (hospital variables, patient variables, arrest variables, and outcome variables) after resuscitation events, it has been possible to gather data in a standardized fashion. Recent studies,^{20–22} availing themselves of Utstein template and data collection methods, have focused on intra-arrest characteristics that are predictive of survival, but such data are not helpful to the physician or patient attempting to make a preemptive decision about the use of CPR.

Our study aims to determine variables predictive of non-survival after in-hospital cardiac arrest and resuscitation to create a score that can be clinically useful to physicians and their patients.

Methods

Setting. The center is a level one trauma center affiliated with Geisel Medical School at Dartmouth with average yearly admission of 20,000 patients. The hospital is a regional tertiary-care hospital for northern New England, providing neurosurgery, cardiovascular surgery, and critical care to the region. The facility includes 36 critical care beds for mechanically ventilated patients and 389 inpatient acute care beds with telemetry monitoring available for all beds. At the time of the study, the resuscitation team, comprising trained and certified internal medicine interns, senior internal medicine and anesthesia residents, nurses, and respiratory therapists, was notified and assembled via paging by the hospital switchboard at the time of cardiac arrest.

Patient selection. Individuals were identified retrospectively from the CPR committee log of in-hospital cardiopulmonary arrests. Per hospital protocol, all cardiopulmonary arrests are called into the hospital switchboard, activating a *code blue* protocol, which notifies the code team and logs the occurrence of the arrest. Cardiac arrest was defined “the cessation of cardiac mechanical activity, confirmed by the absence of a detectable pulse, unresponsiveness, and apnea”.¹⁹ The study cohort consisted of all consecutive patients aged 18 years

and older with an in-hospital cardiac arrest and attempted resuscitation. Syncope, seizures, and primary respiratory arrests were excluded due to increased survival rates of those patient populations with early intervention. An individual was only entered into our database one time, regardless of the number of times they suffered a cardiac arrest. Patients whose resuscitation began outside of the hospital were excluded.

Sample size calculation. Assuming unequal groups (based on published studies^{2,3} and review of our internal survival data, we predicted a 20% survival rate after cardiac arrest), 308 enrolled patients were needed for the study to have a statistical power of 80% to detect a significant difference with respect to history of congestive heart failure or renal failure with a two-sided α -level of 0.05. We determined the study size and power only for congestive heart failure and renal failure because they were the only parameters with adequate published data for a two-sided α -level of 0.05. We attempted to compensate for the lack of data with which to power the study by significantly overenrolling patients (a total of 470 were enrolled in our study).

Data collection. We retrospectively reviewed medical and nursing records of all adult inpatient CPR attempts at our institution between January 2003 and December 2005. A single trained chart abstractor reviewed each medical record. Admission variables were recorded on a structured data collection sheet designed for this study. We used admission variables (values obtained within 24 hours of admission) because we expect conversations about CPR and therefore the use of our rule, to take place on admission. We prespecified all variables by developing a list of variables identified in the literature as varying significantly between survivors and nonsurvivors.^{16–18,21,23} All admission variables were defined as precisely as possible (see Appendix) prior to data collection. Admission variable definitions were adapted when possible from those used in previous investigations.²³ To minimize bias associated with the unavailability of data in patient subgroups, we imputed a value of normal when a physiologic value was missing.

The primary outcome measured was nonsurvival to hospital discharge. The study protocol was approved by the institutional review board, the Committee for the Protection of Human Subjects, at Dartmouth College.

Development of the clinical prediction rule. Two different techniques, linear discriminant analysis (LDA) and logistic regression (LR), were considered. Both techniques are established methods of generating prediction rules. The slight differences in the techniques allow each to occasionally outperform the other. In theory, if the feature covariance matrices for each of the two sets of patients are unequal, there may be a slight advantage to using LR over LDA. However, empirical evidence suggests that this covariance matrix test is not always predictive.^{24,25} We therefore computed clinical prediction rules using both LDA and LR and compared their performance.

To remain consistent with previous work, we defined a positive outcome as not surviving to discharge.²⁶ A true positive



(TP) is a patient who does not survive to discharge who was predicted not to survive. A true negative (TN) is a patient who survives who was predicted to survive. A false positive (FP) is a patient who lives but was predicted to die. A false negative (FN) is a patient who dies but was predicted to live. The specificity measures the percentage of patients who lived and who were predicted to live (specificity = $TN / (TN + FP)$). The sensitivity measures the percentage of patients who did not survive who were predicted to not survive (sensitivity = $TP / (TP + FN)$). We decided it was most important to minimize the number of FPs. Therefore, we maximized the specificity. A specificity of 1 means that there were no patients predicted to die who actually lived.

The dataset consisting of 470 patients was divided into derivation and validation cohorts. A random sample of 330 patients was assigned to the derivation cohort, which was used for developing the prediction rule (Fig. 1). After we constructed the model, we evaluated its performance on the validation cohort.

Twenty-six of 30 initially collected features were used with LDA to create the clinical prediction rule. S3 gallop and abnormal PaCO₂ were excluded due to insufficient data. Independence or dependence with ADLs was removed after analysis revealed that the act of assessing ADL status, not the status itself, was predictive of survival. Using the derivation cohort, a search over all possible 10-feature combinations of the 26 features (approximately 5.3 million combinations) was performed. Each set of 10 features was evaluated by performing 1,000 splits of the derivation cohort into a training set containing 90% of the patients in the cohort and a testing set containing the remaining 10%. For each split, LDA

was used to generate significance weights for each feature and a temporary threshold was chosen to identify all survivors on the training set. The choice to identify all survivors compromised sensitivity but resulted in a desired low FP rate. The average performance over the 1,000 randomly chosen test sets was used as a criterion to rank each set of 10 features.

The best performing 10-feature rule was identified and normalized to create an integer classifier with all feature weights falling between 0 and 5 (inclusive). To increase the usability and adaptability of the tool by the health-care team, all initially negative weights were converted to positive weights by replacing each feature with a negative weight with an equivalent *absent* feature with the same weight magnitude, albeit positive (eg, angina pectoris had an initial weight of -4, so we added a feature *no angina pectoris* with a weight of +4). This weight inversion required that the thresholds be shifted by an equivalent amount. The final thresholds reported in this study (≤ 7 and ≥ 9) were manually selected by examining the data. Patients with a score of 7 or lower are likely to survive to discharge, patients with a score of 9 or above are not likely to survive to discharge, and no prediction is made for patients who score between the thresholds. A total of 17 patients (12%) of the validation cohort and 58 patients (12%) of all data (derivation and validation) have a score of 8. The performance of this rule was evaluated against the validation cohort, and the results were compared against other clinical prediction rules.

We also considered the technique of LR. The entire data set was analyzed with the LR functions as implemented in the statistical computing software R.²⁷ Logistic regression was constructed using the generalized linear model (glm) function in R, where features were iteratively removed until only statistically significant features remained. The binomial logit model was used, and calculations took four Fisher Scoring iterations. Four features were identified with *P*-values less than 0.05. The classifier was normalized to integer weights, and thresholds were manually selected to optimize sensitivity and specificity. Since the data were not divided into derivation and validation cohorts, the performance of LR was judged using the entire dataset. Given that we are trying to optimize specificity, it is most fair to compare the LDA model to an LR model with threshold chosen to approximately match the specificity of the LDA-derived rule.

Results

Characteristics of the study population. A total of 470 individual attempts at CPR after cardiopulmonary arrest were reviewed. Overall, 25.7% survived to hospital discharge. In the derivation cohort, the mean age was 67.2 years (standard deviation, 14.8 years), 58.5% were men, and 85 of 330 or 25.8% survived to hospital discharge. In the validation cohort, the mean age was 67.0 (standard deviation, 15.7 years), 51.4% were men, and 36 of 140 or 25.7% survived to hospital discharge. No significant differences in baseline characteristics between the two cohorts were observed (Table 1).

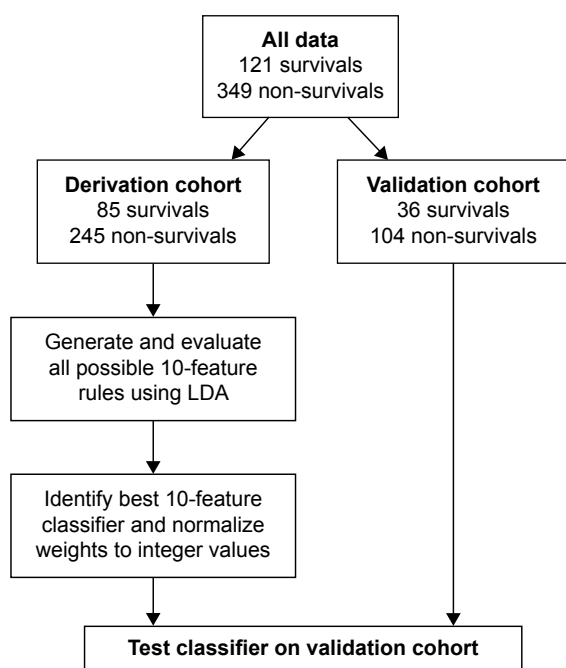


Figure 1. Flow chart of patients included in data analysis.

**Table 1.** Baseline characteristics of the derivation and validation cohorts.

CHARACTERISTIC	NUMBER OF PATIENTS		% OF PATIENTS		P-VALUE	CHI-SQUARE SCORE
	DERIVATION COHORT	VALIDATION COHORT	DERIVATION COHORT	VALIDATION COHORT		
Male sex	193	72	58%	51%	0.158	1.990
Age > 70	148	67	45%	48%	0.549	0.359
Independent ADLs	160	76	48%	54%	0.250	1.323
Not-completely-independent ADLs	128	47	39%	34%	0.285	1.145
PMH CVA	37	15	11%	11%	0.875	0.025
CRI/ESRD	71	29	22%	21%	0.846	0.038
Angina pectoris	102	36	31%	26%	0.258	1.279
CHF (III or IV)	98	36	30%	26%	0.382	0.765
PMH MI	73	24	22%	17%	0.223	1.487
Cancer	82	32	25%	23%	0.645	0.212
Cirrhosis	9	6	3%	4%	0.379	0.773
Dementia	13	4	4%	3%	0.566	0.330
Respiratory insufficiency	114	47	35%	34%	0.839	0.041
Immunocompromised	8	4	2%	3%	0.786	0.074
Sepsis	25	9	8%	6%	0.661	0.193
Pneumonia	46	19	14%	14%	0.916	0.011
Recent MI	90	41	27%	29%	0.656	0.198
CVA	14	8	4%	6%	0.490	0.477
Coma	13	3	4%	2%	0.326	0.965
Ventilation	145	71	44%	51%	0.178	1.817
Hypotension	94	35	28%	25%	0.439	0.599
S3 gallop	1	0	0%	0%	0.514	0.425
Oliguria	4	2	1%	1%	0.848	0.037
Pulmonary edema	73	37	22%	26%	0.313	1.017
Abnl BUN	48	23	15%	16%	0.602	0.272
Abnl Cr	136	51	41%	36%	0.333	0.939
Abnl pH	75	28	23%	20%	0.513	0.427
Abnl PaCO ₂	95	38	29%	27%	0.717	0.131
Abnl PaO ₂	23	11	7%	8%	0.734	0.115
Abnl bicarb	31	11	9%	8%	0.593	0.285
Deceased	245	104	74%	74%	0.992	0.000

In χ^2 univariate analysis of the derivation cohort, the presence of angina pectoris, hypotension, abnormal pH, and abnormal bicarbonate were the only characteristics that had a statistically significant difference between patients who survived to discharge and those who did not (Table 2). Angina pectoris was found to be protective while hypotension, abnormal pH, and abnormal bicarbonate were significant risk factors for nonsurvival to hospital discharge. There was no significant association between mortality and the other variables.

Description of the clinical prediction rule. We define the Dartmouth Score (DS) as the best 10-feature clinical prediction rule generated using LDA (Table 3). The rule includes

both protective features and those indicative of nonsurvival. It achieves a specificity of 82.4% and a sensitivity of 42.7% on the validation cohort. In contrast, the LR-derived rule obtained when the threshold is set to approximate the same specificity (83%) achieves a lower sensitivity and a higher FN rate than the DS (Table 4).

In the DS, the features of age (greater than 70 years of age), history of cancer, previous cardiovascular accident or CVA, presence of coma, hypotension, abnormal PaO₂, and abnormal bicarbonate were identified as the best predictors of nonsurvival. Angina, dementia, and chronic respiratory insufficiency were selected as protective features.

**Table 2.** Univariate analysis of clinical characteristics and survival in the derivation cohort.

CHARACTERISTIC	NUMBER OF PATIENTS (%)		P-VALUE
	DERIVATION COHORT N = 330	VALIDATION COHORT N = 140	
	N = 330	N = 140	
Male sex	193 (58)	72 (51)	0.158
Age > 70	148 (45)	67 (48)	0.549
Independent ADLs	160 (48)	76 (54)	0.25
Not-completely-independent ADLs	128 (39)	47 (34)	0.285
PMH CVA	37 (11)	15 (11)	0.875
CRI/ESRD	71 (22)	29 (21)	0.846
Angina pectoris	102 (31)	36 (26)	0.258
CHF (III or IV)	98 (30)	36 (26)	0.382
PMH MI	73 (22)	24 (17)	0.223
Cancer	82 (25)	32 (23)	0.645
Cirrhosis	9 (3)	6 (4)	0.379
Dementia	13 (4)	4 (3)	0.566
Respiratory insufficiency	114 (35)	47 (34)	0.839
Immunocompromised	8 (2)	4 (3)	0.786
Sepsis	25 (8)	9 (6)	0.661
Pneumonia	46 (14)	19 (14)	0.916
Recent MI	90 (27)	41 (29)	0.656
CVA	14 (4)	8 (6)	0.49
Coma	13 (4)	3 (2)	0.326
Ventilation	145 (44)	71 (51)	0.178
Hypotension	94 (28)	35 (25)	0.439
S3 gallop	1 (<1)	0 (0)	0.514
Oliguria	4 (1)	2 (1)	0.848
Pulmonary edema	73 (22)	37 (26)	0.313
Abnl BUN	48 (15)	23 (16)	0.602
Abnl Cr	136 (41)	51 (36)	0.333
Abnl pH	75 (23)	28 (20)	0.513
Abnl PaCO ₂	95 (29)	38 (27)	0.717
Abnl PaO ₂	23 (7)	11 (8)	0.734
Abnl bicarb	31 (9)	11 (8)	0.593
Deceased	245 (74)	104 (74)	0.992

Notes: The four features in bold demonstrated a statistically significant difference between patients who survived and did not survive (via χ^2 analysis at the 0.05 level).

Table 3. The DS 10-feature clinical prediction rule.

CLINICAL FEATURE	WEIGHTED SCORE
Age > 70	2
No angina pectoris	4
No dementia	1
No respiratory insufficiency	2
CVA	5
Hypotension	3
Abnl PaO ₂	3
Abnl bicarb	3
Coma	2
Cancer	1

Table 4. Test characteristics of LR analysis classifier.

PERFORMANCE OF LR CLASSIFIER	
Specificity	0.83
Sensitivity	0.33
FNrate	0.67
LRP	1.99
LRN	0.80
PPV	0.85
NPV	0.30

Notes: Included features: abnormal pH, hypotension, age > 70 years and chronic stable angina.

Abbreviations: FNrate, false negative rate; LRP, likelihood ratio of a positive result; LRN, likelihood ratio of a negative result; PPV, positive predictive value; NPV, negative predictive value.



Development of thresholds for utilization. Setting the survival threshold at ≤ 7 and the nonsurvival threshold at ≥ 9 allowed us to predict the outcome in 88% of patients in our validation cohort. For 12% of the patients, there was insufficient information, given the clinical features, to make a prediction. In these instances, rather than force a prediction, the rule states that the outcome is uncertain.

Comparison with other scores. We compared our rule's performance to the performance of previously published clinical prediction rules (PAM,²² PAR,¹⁶ MPI¹⁷) on our validation cohort (Table 5). Compared with previously published rules,

Table 5. Comparison of test characteristics. The DS with other published scores.

	TEST
PAM	
Specificity	0.78
Sensitivity	0.30
FNrate	0.70
LRP	1.34
LRN	0.90
PPV	0.80
NPV	0.28
<i>P</i> -value	0.382
PAR	
Specificity	0.86
Sensitivity	0.18
FNrate	0.82
LRP	1.32
LRN	0.95
PPV	0.79
NPV	0.27
<i>P</i> -value	0.548
MPI	
Specificity	0.89
Sensitivity	0.24
FNrate	0.76
LRP	2.16
LRN	0.86
PPV	0.86
NPV	0.29
<i>P</i> -value	0.099
DS Cutoff 7, 9	
Specificity	0.82
Sensitivity	0.43
FNrate	0.57
LRP	2.42
LRN	0.70
PPV	0.86
NPV	0.35
<i>P</i> -value	0.010

Abbreviations: FNrate, false negative rate; LRP, likelihood ratio of a positive result; LRN, likelihood ratio of a negative result; PPV, positive predictive value; NPV, negative predictive value; *P*-value, χ^2 *P*-value for clinical prediction vs actual outcome.

our score achieves the highest sensitivity and is most predictive, having the highest positive and negative prediction values, while maintaining relatively similar specificity and FN rates. Interestingly, the previously published morbidity scores PAM, PAR, MPI do not show a statistically significant difference between the scores of those who survive to hospital discharge and those who do not (*P*-values for χ^2 for MPI 0.10, PAM 0.38, PAR 0.55). There is a statistically significant correlation between the DS of patients who are discharged alive and those who are not (*P*-value for χ^2 for DS is 0.01). It is important to note that despite our use of separate derivation and validation cohorts, one would reasonably expect our rule to outperform previous rules on our dataset given that our patient demographics are likely slightly different from those used to create previous rules. Follow-up studies will be informative with respect to how well our rule generalizes.

Discussion

Discussion of code status has become a routine part of many hospital admissions, but is still performed without sufficient discussion of or knowledge about the patient's chance of surviving resuscitation. We used two statistical techniques to create a simple but clinically useful prediction tool. The DS uses information easily obtainable on admission to provide physicians and their patients individualized information about their probability of survival after in-hospital cardiopulmonary arrest and attempted resuscitation.

Our dataset is the largest to date used to develop a clinical prediction rule for nonsurvival after in-hospital cardiac arrest. We used standardized definitions of medical diagnoses, physical findings, and laboratory tests to determine each individual's features. We combined our comprehensive retrospective chart review with rigorous computational methods to create a relatively sensitive and specific score with a statistically significant correlation between predicted and actual outcomes. We attempted to maximize specificity since most physicians would prefer to attempt several unsuccessful resuscitations rather than risk withholding resuscitation from a single patient in whom it would be successful. Our two-threshold prediction rule is more sensitive than other previously published scores. Our prediction rule has the additional advantage that it can indicate when there is insufficient information to make a prediction. Given the complexity of many patients' medical state, the identification of a *gray zone* is clinically reasonable.

As mentioned above, our study population (derivation plus validation cohorts) had an average of 25.7% of patients survive CPR to hospital discharge. The DS was able to provide more patient-specific information about chances of surviving to hospital discharge. Patients with a score of 7 or lower on the DS had a 35% chance of surviving to hospital discharge after CPR, while those patients with a score of 9 or higher had a less than 12% chance of surviving to hospital discharge after CPR. A χ^2 statistic shows that these distributions are different



with a P -value of 1×10^{-6} . Clinically, the difference in survival rate may seem relevant to some patients and providers and less relevant to others, based on their personal beliefs and knowledge of and interpretation of statistics. This information may be helpful to clinicians when attempting to provide patients and their families personalized, evidence-based numbers about survival with which to inform decision making.

Our prediction rule has reasonable face validity in addition to our successful empirical validation. The multifaceted nature of the relevant medical phenomena makes it difficult to fully rationalize the inclusion of each clinical variable into our prediction rule. In the next few paragraphs, we propose potential medical justification to support our rule's inclusion of several clinical variables. These ideas are intended to spur discussion and are not meant as definitive explanations.

Many of the features of our prediction rule (age > 70 years, chronic stable angina pectoris, dementia, CVA, cancer, comatose state and hypotension) are included as risk factors in previous mortality scores (Table 6). Angina pectoris is included as

a risk factor in PAM and MPI but is a protective factor in our study. This difference may be because of how angina pectoris was defined; we were more rigorous in our definition of angina pectoris and did not include unstable angina as a feature. Chronic, stable angina pectoris may be a surrogate marker for VT arrest, which is known to lead to better survival rates than other forms of cardiac arrest.²⁸

Dementia is included as a risk factor in MPI but is protective in our study. Our study had far fewer patients with dementia than expected (3.6% of the patients in our sample had dementia, compared to a national prevalence of dementia in the elderly of 13.9%).²⁹ We suspect that our finding reflects that only a subsection of healthier demented patients undergo CPR as increased use of advanced directives and living wills prevent resuscitation in patients with end-stage dementia.

Chronic respiratory insufficiency is unique to our score. Patients with respiratory insufficiency are more likely to be exposed to theophylline and beta-adrenergic agonists, which can cause ventricular ectopy including ventricular tachycardia. In addition, chronic obstructive pulmonary disease is associated with prolonged QT, which can degenerate into torsades de pointes. Increased survival after CPR for patients with chronic respiratory insufficiency may reflect these more treatable arrhythmias.

Abnormal laboratory results of partial pressure of oxygen in arterial blood (PaO_2) and serum bicarbonate are also unique to our score. Review of patients with abnormal PaO_2 found hypoxia significant enough to require ventilation and is therefore in line with prior scores use of indicators of acute respiratory insufficiency (ventilator-dependent and pneumonia) as risk factors for nonsurvival. Review of patients with abnormal serum bicarbonate indicated that 91% of patients with abnormal levels suffered from severe acidemia, with the remaining patients having chronic respiratory acidosis. Low serum bicarbonate may thus be a proxy for organ infarction (lactic acidosis), diabetic ketoacidosis, renal failure, or fatal toxic ingestions.

Poor functional status has been shown to correlate with poor outcomes in other studies. We had hoped to incorporate functional status in our score, but the lack of data reflecting functional status in the sicker, intensive care-based population, prevented us from doing so. We were unable to collect data on functional status or neurological function at discharge, and therefore, our rule can only predict survival to discharge and not the quality of life expected at discharge.

Our rule was derived using data from a patient population that underwent CPR. Patients with DNR orders who did not undergo CPR were not captured in our study due to the retrospective nature of data collection. Hence, our rule is biased toward patients who opted against a DNR order.

The DS was developed based on data collected at a rural, academic, tertiary care center serving a largely Caucasian population. Differences in survival after CPR based on location and size of hospital as well as race have been documented.³ The DS should be evaluated outside our institution. The score

Table 6. Comparison of the DS with previously published decision rules.

COMPARISON OF DS WITH PAM, PAR, AND MPI SCORES				
	DS	PAM	PAR	MPI
Age > 70	2		2	1
Angina pectoris		1		1
No angina pectoris	4			
Dementia				2
No dementia	1			
Respiratory insufficiency				
No respiratory insufficiency	2			
CVA	5	1		2
Hypotension	3	3		3
Abnl PaO_2	3			
Abnl bicarb	3			
Coma	2	1		1
Cancer	1	3		2
Metastatic cancer			10	
Non-metastatic cancer			3	
Homebound		3	5	2
Heart failure		1		1
Cirrhosis		1		
Sepsis		1	5	1
Pneumonia		3	3	2
Acute MI		1	-2	1
Ventilated		1		1
Gallop		1		1
Oliguria		1		1
Abnl creatinine		3	3	2
Cutoff	≤ 7 and ≥ 9	> 6	> 7	> 6



was based on data collected retrospectively and validated with an independent validation cohort. Due to the rarity of in-hospital cardiopulmonary arrest, prospective validation of the tool is impractical. Validation retrospectively at multiple centers would provide further evidence as to the accuracy and clinical utility of the DS. Our score may be clinically useful after it is validated by other cohorts.

The complex physiologic process of cardiac arrest, resuscitation, and recovery makes it unlikely that a handful of features will be able to predict outcomes with extremely high accuracy. However, the DS may be a useful addition to medical expertise and clinical judgment in evaluating and communicating an individual's probability of survival after in-hospital cardiopulmonary arrest. Our model may provide helpful information to guide physicians and patients in shared decision making on this important subject.

Author Contributions

Conceived and designed the experiments: HR. Analyzed the data: HR, SM, RL. Wrote the first draft of the manuscript: HR. Contributed to the writing of the manuscript: SM, RL. Agree with manuscript results and conclusions: HR, SM, RL. Jointly developed the structure and arguments for the paper: HR, RL. Made critical revisions and approved final version: HR, SM, RL. All authors reviewed and approved of the final manuscript.

REFERENCES

1. Kouwenhoven W, Jude J, Knickerbocker G. Closed-chest cardiac massage. *JAMA*. 1960;173:1064–1067.
2. Goldberger ZD, Chan PS, Berg RA, et al; American Heart Association Get With The Guidelines—Resuscitation (formerly National Registry of Cardiopulmonary Resuscitation) Investigators. Duration of resuscitation efforts and survival after in-hospital cardiac arrest: an observational study. *Lancet*. 2012;380:1473–1481.
3. Girotra S, Nallamothu BK, Spertus JA, et al; American Heart Association Get with the Guidelines—Resuscitation Investigators. Trends in survival after in-hospital cardiac arrest. *N Engl J Med*. 2012;367:1912–1920.
4. Mirza A, Kad R, Ellison NM. Cardiopulmonary resuscitation is not addressed in the admitting medical records for the majority of patients who undergo CPR in the hospital. *Am J Hosp Palliat Care*. 2005;22(1):20–25.
5. Krumholz HM, Phillips RS, Hamel MB, et al. Resuscitation preferences among patients with severe congestive heart failure: results from the SUPPORT project. *Circulation*. 1998;98:648–655.
6. Hofmann JC, Wenger NS, Davis RB, et al. Patient preferences for communication with physicians about end-of-life decisions. *Ann Intern Med*. 1997;127:1–12.
7. Phillips RS, Wenger NST, Teno J, et al. Choices of seriously ill patients about cardiopulmonary resuscitation: correlates and outcomes. *Am J Med*. 1996;100:128–137.
8. Haidet P, Hamel MB, Davis RB, et al. Outcomes, preferences for resuscitation, and physician-patient communication among patients with metastatic colorectal cancer. *Am J Med*. 1998;105:222–229.
9. Hakim RB, Teno JM, Harrell FE Jr, et al. Factors associated with do-not-resuscitate orders: patients' preferences, prognoses, and physicians' judgments. *Ann Intern Med*. 1996;125:284–293.
10. Cammer Paris BE, Carrion VG, Meditch JS, Capello CF, Mulvihill MN. Roadblocks to do-not-resuscitate orders: a study in policy implementation. *Arch Intern Med*. 1993;153:1689–1695.
11. Eliasson AH, Parker JM, Shorr AF, et al. Impediments to writing do-not-resuscitate orders. *Arch Intern Med*. 1999;159:2213–2218.
12. Christakis NA, Iwashyna TJ. Attitude and self-reported practice regarding prognostication in a national sample of internists. *Arch Intern Med*. 1998;158:2389–2395.
13. Miller DL, Gorbien MJ, Simbartl LA, Jahnigen DW. Factors influencing physicians in recommending in-hospital cardiopulmonary resuscitation. *Arch Intern Med*. 1993;153:1999–2003.
14. Schonwetter RS, Walker R, Kramer DR, Robinson BE. Resuscitation decision making in the elderly: the value of outcome data. *J Gen Intern Med*. 1993;8:295–300.
15. Murphy DJ, Burrows D, Santilli S, et al. The influence of the probability of survival on patients' preferences regarding cardiopulmonary resuscitation. *NEJM*. 1994;330:545–549.
16. George AL, Folk BP, Crecelius PL, Campbell WB. Pre-arrest morbidity and other correlates of survival after in-hospital cardiopulmonary arrest. *Am J Med*. 1989;87:28–34.
17. Ebell MH. Prearrest predictors of survival following in-hospital cardiopulmonary resuscitation; a meta-analysis. *J Fam Pract*. 1992;34:551–558.
18. Dautzenberg PL, Broekman TC, Hooyer C, Schonwetter RS, Duursma SA. Review: patient-related predictors of cardiopulmonary resuscitation of hospitalized patients. *Age Ageing*. 1993;22:464–475.
19. Cummins RO, Chamberlain D, Hazinski MF, et al. Recommended guidelines for reviewing, reporting, and conducting research on in-hospital resuscitation: the in-hospital 'Utstein Style': a statement for healthcare professionals from the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian Resuscitation Council, and the Resuscitation Councils of Southern Africa. *Circulation*. 1997;95:2213–2239.
20. van Walraven C, Forster AJ, Parish DC, et al. Validation of a clinical decision aid to discontinue in-hospital cardiac arrest resuscitations. *JAMA*. 2001;285:1602–1606.
21. Brindley PG, Markland DM, Mayers I, Kutsogiannis DJ. Predictors of survival following in-hospital adult cardiopulmonary resuscitation. *CMAJ*. 2002;167:343–348.
22. Tok D, Keles GT, Toprak V, Topcu I. Assessment of in-hospital cardiopulmonary resuscitation using Utstein Template in a University hospital. *Toboku J Exp Med*. 2004;202:265–273.
23. Ballew KA, Philbrick JT, Caven DE, Schorling JB. Predictors of survival following in-hospital cardiopulmonary resuscitation. *Arch Intern Med*. 1994;154:2426–2432.
24. Lei P, Koehly L. Linear discriminant analysis versus logistic regression: a comparison of classification errors in the two-group case. *J Exp Educ*. 2003;72:25–49.
25. Meshbane A, Morris JD. *Predictive Discriminant Analysis Versus Logistic Regression in Two-Group Classification Problems*. New York: American Educational Research Association; 1996.
26. Bowker L, Stewart K. Predicting unsuccessful cardiopulmonary resuscitation (CPR): a comparison of three morbidity scores. *Resuscitation*. 1999;40:89–95.
27. R Development Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2010.
28. Marwick T, Case C, Siskind V, Woodhouse S. Prediction of survival from resuscitation: a prognostic index derived from multivariate logistic model analysis. *Resuscitation*. 1991;22:129–137.
29. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. *Neuroepidemiology*. 2007;29:125–132.



Appendix

Precise definitions of all features assessed in creation of the DS. *Activities of Daily Living* include eating, dressing, grooming, toileting, bathing, transferring, walking.

Congestive Heart Failure is defined as NYHA Class III or IV Class III: Symptoms (fatigue, palpitation, dyspnea, or angina) with minimal activity. Class IV: Unable to do physical activity without discomfort. Symptoms of cardiac insufficiency (fatigue, palpitation, dyspnea, or angina) at rest.

Cirrhosis is defined as elevation of both aspartate aminotransferase and alanine aminotransferase levels <300 IU/L with any one of the following clinical findings consistent with cirrhosis: ascites, esophageal varices, or jaundice.

An *organ transplant* is defined as transplant of any organ other than cornea or bone marrow.

Chronic respiratory insufficiency is defined as diagnosis of chronic obstructive pulmonary disease, pulmonary fibrosis, restrictive lung disease, or home O_2 use documented.

Immunocompromised state is defined as the presence of HIV, AIDS, IgA deficiency, long-term steroid, or immunosuppressant therapy.

For a diagnosis of *sepsis*, all of the following criteria are required: (1) clinical suspicion of infection, (2) temperature >38.3 or <35.6 , (3) pulse >90 beats per minute and (4) respiratory rate >20 breaths per minute.

A diagnosis of *pneumonia* requires roentgenographic evidence of pneumonia plus any one of the following: (1) shortness

of breath; (2) tachypnea; (3) increased alveolar-arterial oxygen tension gradient; (4) purulent sputum production; (5) leukocytosis; (6) fever.

Myocardial infarction is defined as (1) characteristic elevation of cardiac markers and (2) EKG changes consistent with acute myocardial infarction.

Diagnosis of prior *cerebrovascular accident* includes patients with definite, highly probable or probable stroke, including thrombotic, embolic, or hemorrhagic cerebrovascular events as well as subarachnoid hemorrhage.

Hypotension is defined as systolic blood pressure <90 mmHg, use of vasopressor agents, or intra-aortic balloon pump or ventricular assist device to maintain blood pressure.

Comatose state is defined as pathological unconsciousness in which the patient is unaware of self or environment and is unarousable.

Oliguria is defined as <300 cc/day or <12.5 cc/hour urine output.

Dementia, *cancer*, and *chronic angina pectoris* were noted if they were found on the problem list or past medical history section of the admission note.

All laboratory values were recorded numerically and converted to normal or abnormal based on the usual reference ranges for the general population, which was defined as the prediction interval of values that 95% (or two standard deviations) of the population fall into.