

Factors Associated With Neurologically Intact Survival for Patients With Acute Heart Failure and In-Hospital Cardiac Arrest

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Background—Hospitalized patients with heart failure are at risk for cardiac arrest. The ability to predict who may survive such an event with or without neurological deficit would enhance the information on which patients and providers establish resuscitative preferences.

Methods and Results—We identified 13 063 adult patients with acute heart failure who had cardiac arrest at 457 hospitals participating in the National Registry of Cardiopulmonary Resuscitation between January 1, 2000 and December 31, 2007. Neurological status was determined on admission and discharge by cerebral performance category with neurologically intact survival (NIS)=cerebral performance category 1 (no) or 2 (moderate dysfunction) and non-NIS=cerebral performance category 3 (severe dysfunction), 4 (coma), or 5 (brain death). Factors available prearrest (demographics, preexisting conditions, and interventions in-place) were assessed for association with NIS using multivariable logistic regression, initially without then with adjustment for arrest-related variables and hospital characteristics. NIS occurred in 2307 patients (17.7%) and was associated by adjusted odds ratio with 18 prearrest factors; 4 positively and 14 negatively. The association (odds ratio; 95% CI) was strongest for 4 specific variables: acute stroke (0.38; 0.25 to 0.58), history of malignancy (0.49; 0.39 to 0.63), vasopressor use (0.50; 0.43 to 0.59), and assisted or mechanical ventilation (0.53; 0.45 to 0.61).

Conclusions—A number of prearrest factors seem to be associated with NIS, the majority inversely. Consideration of these before cardiac arrest could enhance the resuscitative decision-making process for patients with acute heart failure. (*Circ Heart Fail.* 2009;2:572-581.)

Key Words: acute heart failure ■ cardiac arrest ■ cerebral performance category ■ neurologically intact survival

Chronic heart failure (HF) affects nearly 1 in 60 individuals in the United States and is the leading cause of hospitalization for those ≥ 65 years.¹ Although prognosis has improved over the past 4 decades, survival for patients with HF remains poor, with 30-day, 1-year, and 5-year mortality rates in excess of 10%, 30%, and 60%, respectively.²⁻⁴ For those patients who suffer acute decompensation, risk is also relatively high with in-hospital mortality estimates ranging from 1.8% to 8.9%.^{2,5,6}

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More than 80% of HF-related deaths occur among the elderly, the majority of which are due to sudden cardiac arrest.⁷ Prognostication based on individual variables such as blood pressure and renal function and the use of predictive

models can assist with risk stratification for HF mortality^{2,6,8,9} but provide little information with regard to actual outcomes for those who experience a cardiac arrest. Although previous investigation has shown that most patients with HF would elect to have cardiopulmonary resuscitation performed if they suffered a life-threatening cardiac event, many fear consequential development of long-term neurological disability.^{10,11} Studies on in-hospital cardiac arrest, however, have historically focused on return of spontaneous circulation and survival to hospital discharge as the metrics of success with little attention directed toward the actual neurological status of those who survive.¹²⁻¹⁴ More complete characterization of such outcomes would be particularly useful for patients with HF and could facilitate development of a patient-centered approach to resuscitative goal setting.^{15,16}

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The National Registry of Cardiopulmonary Resuscitation (NRCPR) was developed by the American Heart Association to provide a better understanding of the circumstances surrounding in-hospital cardiac arrest.¹⁷ Although the primary purpose of the NRCPR is quality improvement, it is a robust database that includes objective assessment of neurological status by cerebral performance category (CPC). The CPC is a valid measure that defines function using a simple scale, where CPC-1=good cerebral performance, CPC-2=moderate cerebral disability, CPC-3=severe cerebral disability, CPC-4=coma or vegetative state, and CPC-5=certified brain death.¹⁸ Our objective was to use the NRCPR to identify factors associated (positively or negatively) with CPC-1 or -2 at discharge (henceforth referred to as “neurologically intact survival” [NIS]) for patients with acute HF who suffer an in-hospital cardiac arrest. The primary intent of our study was not to develop a prediction model per se nor was it to determine who would or would not have a cardiac arrest but rather to define a set of objective variables that admitted patients with acute HF (or their caregivers) could consider as they work to establish resuscitative preferences.

Methods

Design

This study was designed as a retrospective cohort analysis of the NRCPR. The NRCPR is a prospective multicenter registry of in-hospital resuscitation for cardiac arrest. Data collection has been ongoing since January 1, 2000, and this analysis includes cases that were entered through December 31, 2007. The database from which this report was derived includes 105 293 pediatric and adult sequential index cardiac arrest events from 531 United States and Canadian medical and surgical hospitals. Access to the database was made possible through a formal request to the Scientific Advisory Board of the American Heart Association. Because the NRCPR is designed to facilitate quality improvement and includes only deidentified data elements, participating hospitals are not required to obtain institutional review board approval or patient informed consent before data collection. Approval for this study, however, was granted by the Human Investigation Committee at Wayne State University with exemption from full board review.

NRCPR Data

The methodology of data collection for the NRCPR has been described more completely elsewhere.^{17,19} In brief, Utstein-style definitions and outcome measures are used to identify cardiac arrest events. Deidentified data elements are then abstracted by specially trained NRCPR-certified research coordinators and entered into a computerized database with precisely defined variables. Variables exist for 6 major categories: facility data, patient demographic data, preevent data, event data, outcome data, and quality improvement data. Case-study methods are used to ensure data accuracy, and all data are managed in a central repository (Digital Innovations, Inc, Forest Hill, Md) with oversight by the American Heart Association.

Data integrity is assessed by a periodic reabstraction process, which involves a random sampling of event records and corresponding NRCPR data sheets. These random samples are derived from participant sites on a quarterly basis and are reviewed for errors by members of the NRCPR advisory board. Software data checks and an Internet-based remediation program support continuous data integrity.

Inclusion and Exclusion Criteria

By design, the NRCPR contains only in-hospital resuscitation events that meet the following definition: a pulseless cardiopulmonary arrest that requires chest compressions, defibrillation, or both, which elicits an emergency resuscitation response by facility personnel and

results in the generation of a resuscitation record.¹⁹ All patients with out-of-hospital cardiac arrest, successful defibrillation by implantable cardioverter-defibrillator and active do not resuscitate orders therefore are excluded from the registry. For this particular study, we limited our analysis to the following: adult patients (age, ≥ 18 years) without trauma or obstetric-related conditions who had acute HF (defined by the NRCPR as a documented diagnosis of acute HF during the index hospital admission), were neurologically intact (ie, CPC-1 or -2) on admission to the hospital, had no advanced directives precluding cardiopulmonary resuscitation or resuscitative intervention, and had complete, accurate data available including CPC at discharge. This resulted in a final study cohort of 13 063 patients from 457 facilities. A flow chart outlining cohort derivation is provided in Figure 1.

Outcome Measure and Data Elements

The outcome measure of interest was NIS (CPC-1 or -2) at hospital discharge.¹⁹ Cases were grouped into those with NIS and those with non-NIS (CPC-3, -4, or -5 or death), and group-wise comparisons were performed. Because our primary intent was to identify factors associated with NIS, which could be used for resuscitative decision making in the prearrest period, we focused our investigation on candidate variables (ie, demographics, preexisting conditions, and interventions in-place) that would be available before onset of a life-threatening cardiac event. Preexisting conditions and interventions in-place (Table 1) were selected a priori for inclusion in our analysis if they were plausibly associated with NIS or if they were known to correlate with improved outcomes and needed to be controlled for in multivariable modeling (eg, cardiac monitoring).^{19–21} Operational definitions for preexisting conditions and interventions in-place can be found in an accompanying on-line supplement (Appendix A).

Statistical Analysis

Data were compiled for candidate variables within the defined study cohort and segregated by outcome (NIS versus non-NIS). Univariate comparison was performed for categorical variables using odds ratios (ORs) and 95% CIs. For continuous data, the mean and SD or median and interquartile range are given and either the *t* test or Wilcoxon test was used as appropriate based on distribution of the data. Potential heterogeneity in unadjusted outcome response was assessed using the Breslow-Day test for subgroups stratified by the presence or absence of preexisting comorbidities (as a composite) and specific, clinically important in-hospital events (individually).

Multivariable logistic regression models were fit using NIS as the main outcome. Candidate variables were included regardless of statistical association on univariate analysis. The first model included only information that would be available to the clinician precardiac arrest whereas the second model included 2 important predictors arising from the actual event (henceforth referred to as “arrest-related variables”) known to be associated with improved outcome: any ventricular fibrillation or pulseless ventricular tachycardia during the arrest and event duration (normalized by natural log transformation).^{13,14,19,21–23} Results of logistic regression analyses are reported as adjusted ORs and corresponding 95% CIs. To evaluate the potential impact of similar patient characteristics and processes of care and to account for potential clustering of events within hospitals, the same variable sets were analyzed using the general estimating equation (PROC GENMOD). Outcome was also assessed as a polytomous occurrence using 3-tier (NIS, survival with significant neurological impairment [CPC-3 or -4], and death or CPC-5) multinomial logistic regression modeling. All analyses were performed using SAS (SAS Institute, Cary, NC) and SPSS (SPSS, Inc, Chicago, Ill) software.

The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Baseline data for the study cohort are presented in Table 2. Of 13 063 patients with acute HF included in the main analysis,

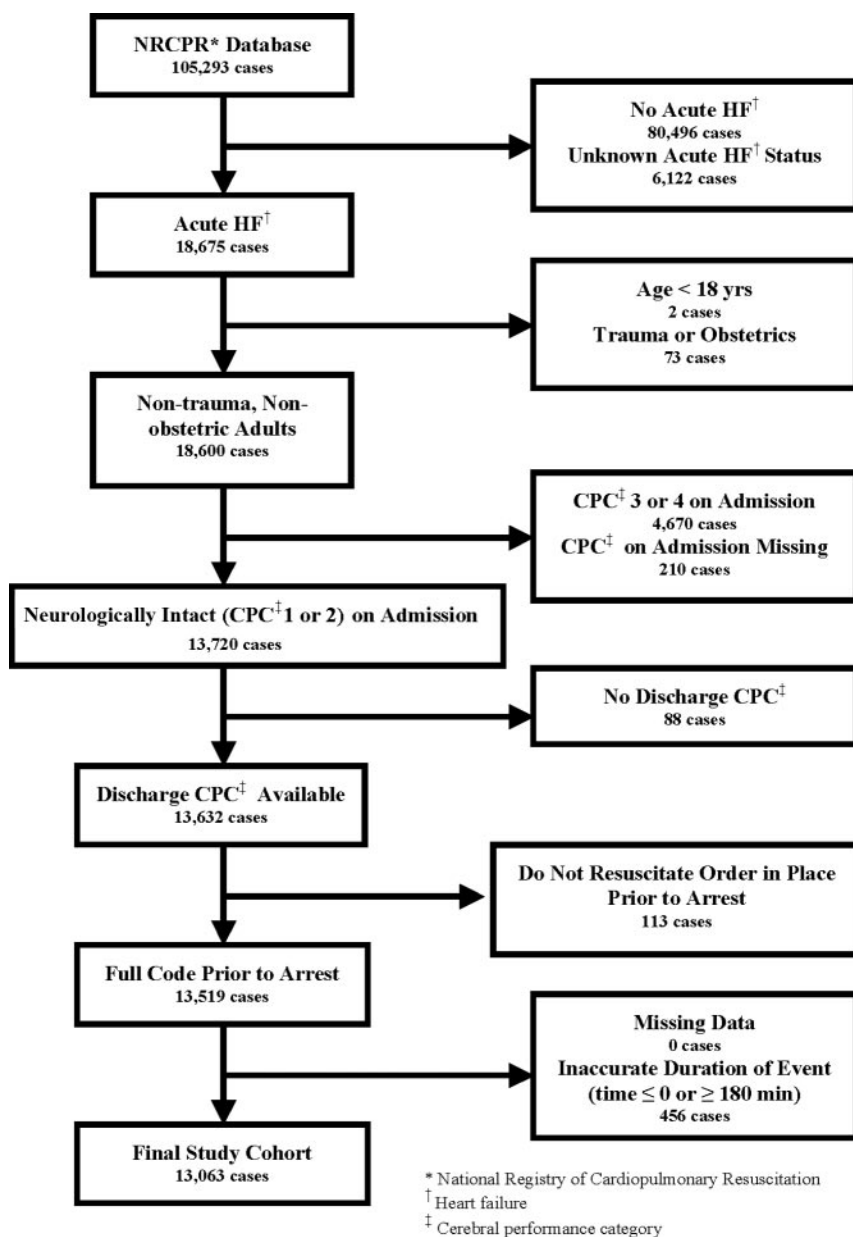


Figure 1. Study cohort derivation flow chart.

6844 (52.4%; 95% CI, 51.5% to 54.3%) survived the initial event and 2608 (20.0%; 95% CI, 19.3% to 20.6%) survived to hospital discharge. Of those who survived to discharge, 2307 (88.5% [17.7% overall]; 95% CI, 87.2% to 89.6% [17.0% to 18.3%]) were neurologically intact. The remaining 10 756 patients were non-NIS, 10 455 (97.2% [80.0% overall]; 95% CI, 96.9% to 97.5% [79.4% to 80.7%]) of whom died in-hospital. Of the 301 (2.8% [2.3% overall]; 95% CI, 2.5% to 3.1% [2.1% to 2.6%]) non-NIS patients discharged alive, 224 (74.4% [1.7% overall]; 95% CI, 69.2% to 79.0% [1.5% to 1.9%]) were CPC-3 and 77 (25.6% [0.6% overall]; 95% CI, 20.9% to 30.8% [0.5% to 0.7%]) were CPC-4.

Univariate data for the comparison of NIS with non-NIS are presented in Table 3 (unadjusted ORs). Patients with NIS were slightly younger (mean age, 67.5 versus 69.7 years; difference of the mean = -2.2 years [95% CI, -2.8 to -1.6]) and more likely to be white (76.4% versus 72.3%; difference

of the proportion = 4.1% [95% CI, 2.1% to 6.0%]). On subgroup analysis, patients without preexisting comorbidities (n=1725) were more likely to have NIS (22.1% versus 17.0%; unadjusted OR=1.39 [95% CI, 1.23 to 1.57]) than those with 1 or more comorbidity (n=11 338). However, with the exception of any ventricular fibrillation or pulseless ventricular tachycardia during the arrest (unadjusted OR=2.52 [95% CI, 1.99 to 3.19] versus 1.56 [1.41 to 1.71]), response characteristics to clinically important in-hospital events were similar (Figure 2).

Multivariable logistic regression data are presented in Table 4 (adjusted ORs). When cardiac monitoring, any ventricular fibrillation or pulseless ventricular tachycardia and log-transformed event duration were controlled for, 4 variables correlated with an increased odds of NIS (no therapeutic interventions, diabetes mellitus at baseline, arrhythmia during the index admission, and pulmonary artery

Table 1. Preexisting Conditions and Interventions In-Place Included in Analysis

Conditions present before the index admission	
Depression in CNS function	
Heart failure	
Myocardial infarction	
Diabetes mellitus	
Hepatic insufficiency	
Malignancy (metastatic or hematologic)	
Conditions diagnosed during the index admission ≥ 4 h before arrest	
Acute stroke	
Acute myocardial infarction	
Arrhythmia	
Pneumonia	
Renal insufficiency	
Septicemia	
Conditions detected <4 h before arrest	
Hypotension/hypoperfusion	
Metabolic/electrolyte abnormality	
Respiratory insufficiency	
Acute nonstroke CNS event	
Interventions in-place before arrest	
Assisted or mechanical ventilation	
Arterial line	
Pacemaker	
Cardiac monitor	
Central venous line	
Pulmonary artery catheter	
Dialysis	
Implantable cardioverter-defibrillator	
Intra-aortic balloon pump	
Continuous infusion therapy with	
Vasopressors (epinephrine, norepinephrine, phenylephrine, or dopamine)	
Dobutamine	
Phosphodiesterase inhibitors (amrinone or milrinone)	
Lidocaine	
Amiodarone	
Procainamide	
Nitroglycerin	
Nitroprusside	

catheter use before arrest) and 14 variables correlated with a decreased odds (age, black race, central nervous system [CNS] depression, malignancy or hepatic insufficiency at baseline, acute stroke, septicemia or renal insufficiency diagnosed during the index admission, hypotension/hypoperfusion or acute nonstroke CNS event within 4-hours of arrest, and continuous infusion of vasopressors or dobutamine, pacemaker use, or assisted or mechanical ventilation before arrest). When the data were reanalyzed looking at only those who survived the initial cardiac arrest, results were unchanged. There was also no important change when the analysis was conducted using the general estimating equation.

Table 2. Baseline Characteristics of Study Cohort

Characteristic	Study Cohort (n=13 063)
Age, y	
Mean (SD)	69.3 (13.9)
Median (IQR)	72 (61–80)
Male sex, n (%)	7688 (58.9)
Race, n (%)	
White	9538 (73.0)
Black	2373 (18.2)
Other	1152 (8.8)
Residence, n (%)	
Home	10 396 (79.6)
Nonhome*	2667 (20.4)
Preexisting conditions, n (%)	
Acute CNS event (nonstroke)	921 (7.1)
Acute stroke	323 (2.5)
Baseline depression in CNS function	1200 (9.2)
Arrhythmia	6436 (49.3)
Diabetes mellitus	5338 (40.9)
Prior Hx of heart failure	6820 (52.2)
Electrolyte or metabolic abnormality	2645 (20.2)
Hepatic insufficiency	962 (7.4)
Hypotension/hypoperfusion	4550 (34.8)
Malignancy	908 (7.0)
Acute myocardial infarction	4187 (32.1)
Prior Hx of myocardial infarction	3847 (29.4)
Pneumonia	2286 (17.5)
Septicemia	1817 (13.9)
Renal insufficiency	5873 (45.0)
Respiratory insufficiency	6617 (50.7)
Interventions in-place, n (%)	
Assisted or mechanical ventilation	3473 (26.6)
Arterial line	1240 (9.5)
Pacemaker	1725 (13.2)
Cardiac monitor	11 277 (86.3)
Central venous line	470 (3.6)
Pulmonary artery catheter	790 (6.0)
No therapeutic interventions	4947 (37.9)
Dialysis	663 (5.1)
Implantable cardioverter-defibrillator	626 (4.8)
Intraaortic balloon pump	388 (3.0)
Continuous infusions	
Vasopressors	3442 (26.3)
Dobutamine	1028 (7.9)
Phosphodiesterase inhibitor	176 (1.3)
Lidocaine	245 (1.9)
Amiodarone	689 (5.3)
Procainamide	19 (0.1)
Nitroglycerin	258 (2.0)
Nitroprusside	22 (0.2)
Any VF or pVT, n (%)	6094 (46.7)
Event duration, min	
Mean (SD)	20.9 (17.7)
Median (IQR)	17.0 (9.0–28.0)

IQR indicates interquartile range; VF, ventricular fibrillation; pVT, pulseless ventricular tachycardia.

*Includes other hospital, rehabilitation center, nursing facility, supervised residence, or hospice.

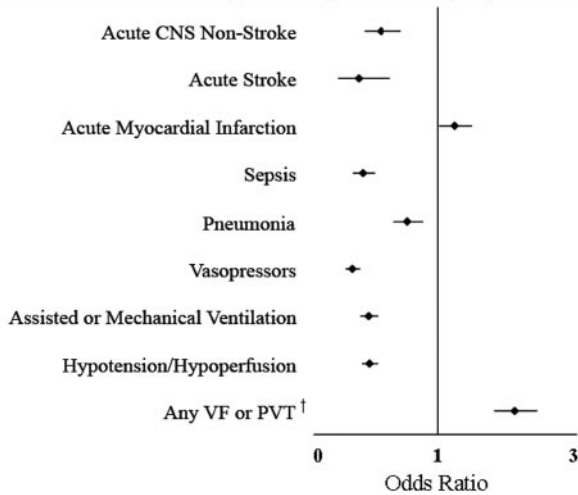
Table 3. Characteristics and Their Association With Neurologically Intact Survival in Unadjusted Analysis

Characteristic	Neurologically Intact Survival (n=2307)	Nonneurologically Intact Survival (n=10 756)	Unadjusted Odds Ratios (95% CI)
Age, y			
Mean (SD)	67.5 (13.2)	69.7 (14.0)	
Median (IQR)	69 (59–78)	72 (61–81)	
Male sex, n (%)	1329 (57.6)	6359 (59.1)	1.06 (0.97–1.17)
Race, n (%)			
White	1762 (76.4)	7776 (72.3)	
Black	343 (14.9)	2030 (18.9)	
Other	202 (8.8)	950 (8.8)	
Residence, n (%)			
Home	1857 (80.5)	8539 (79.4)	1.07 (0.96–1.20)
Nonhome*	450 (19.5)	2217 (20.6)	
Preexisting conditions, n (%)			
Acute CNS event (nonstroke)	99 (4.3)	822 (7.6)	0.54 (0.44–0.67)
Acute stroke	27 (1.2)	296 (2.8)	0.42 (0.28–0.62)
Baseline depression in CNS function	137 (5.9)	1063 (9.9)	0.58 (0.48–0.69)
Arrhythmia	1223 (53.0)	5213 (48.5)	1.20 (1.10–1.31)
Diabetes mellitus	981 (42.5)	4357 (40.5)	1.09 (0.99–1.19)
Prior Hx of heart failure	1185 (51.4)	5635 (52.4)	0.96 (0.88–1.05)
Electrolyte or metabolic abnormality	349 (15.1)	2296 (21.3)	0.66 (0.58–0.74)
Hepatic insufficiency	94 (4.1)	868 (8.1)	0.48 (0.39–0.60)
Hypotension/hypoperfusion	530 (23.0)	4020 (37.4)	0.50 (0.45–0.56)
Malignancy	83 (3.6)	825 (7.7)	0.45 (0.36–0.57)
Acute myocardial infarction	799 (34.6)	3388 (31.5)	1.15 (1.05–1.23)
Prior Hx of myocardial infarction	721 (31.3)	3126 (29.1)	1.11 (1.01–1.22)
Pneumonia	325 (14.1)	1961 (18.2)	0.74 (0.65–0.84)
Septicemia	173 (7.5)	1644 (15.3)	0.45 (0.38–0.53)
Renal insufficiency	865 (37.5)	5008 (46.6)	0.69 (0.63–0.76)
Respiratory insufficiency	977 (42.3)	5640 (52.4)	0.67 (0.61–0.73)
Interventions in-place, n (%)			
Assisted or mechanical ventilation	385 (16.7)	3088 (28.7)	0.50 (0.44–0.56)
Arterial line	197 (8.5)	1043 (9.7)	0.87 (0.74–1.02)
Pacemaker	252 (10.9)	1473 (13.7)	0.77 (0.67–0.89)
Cardiac monitor	2063 (89.4)	9214 (85.7)	1.42 (1.23–1.63)
Central venous line	69 (3.0)	401 (3.7)	0.80 (0.61–1.03)
Pulmonary artery catheter	136 (5.9)	654 (6.1)	0.97 (0.80–1.17)
No therapeutic interventions	1033 (44.8)	3914 (36.4)	1.42 (1.29–1.55)
Dialysis	81 (3.5)	582 (5.4)	0.64 (0.50–0.81)
Implantable cardioverter-defibrillator	94 (4.1)	532 (4.9)	0.82 (0.65–1.02)
Intraaortic balloon pump	69 (3.0)	319 (3.0)	1.01 (0.78–1.31)
Continuous infusions			
Vasopressors	314 (13.6)	3128 (29.1)	0.38 (0.34–0.44)
Dobutamine	136 (5.9)	602 (7.1)	0.69 (0.58–0.84)
Phosphodiesterase inhibitor	34 (1.5)	142 (1.3)	1.12 (0.77–1.63)
Lidocaine	53 (2.3)	192 (1.8)	1.29 (0.95–1.76)
Amiodarone	131 (5.7)	558 (5.2)	1.10 (0.91–1.34)
Procainamide	16 (0.1)	3 (0.03)	0.87 (0.25–3.00)
Nitroglycerin	65 (2.8)	193 (1.8)	1.56 (1.19–2.11)
Nitroprusside	7 (0.3)	15 (0.1)	2.18 (0.89–5.35)

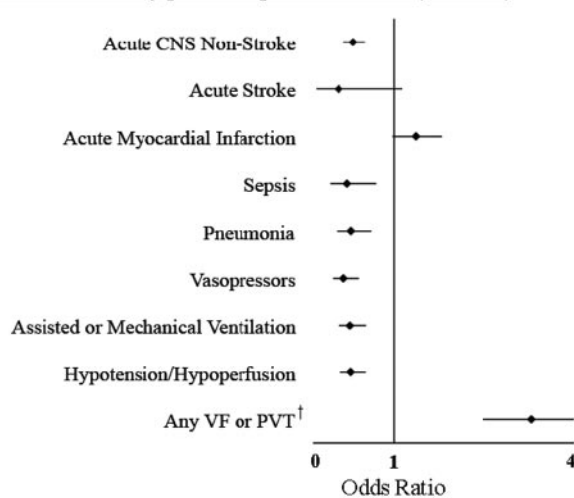
IQR indicates interquartile range.

*Includes other hospital, rehabilitation center, nursing facility, supervised residence, or hospice.

Patients with one or more preexisting co-morbidity* (n = 11,338)



Patients without any preexisting co-morbidities (n = 1725)



*Preexisting co-morbidities include baseline depression in central nervous system function, diabetes mellitus, heart failure, prior myocardial infarction, hepatic insufficiency, malignancy, and/or renal insufficiency.

[†]Difference significant by the Breslow-Day test for heterogeneity ($p = 0.0002$).

Figure 2. Forest plots of neurologically intact survival stratified by the presence or absence of preexisting comorbidities within clinically significant in-hospital event subgroups.

As a logistic regression model, the prearrest variables alone were only moderately predictive of NIS (c statistic=0.69). With the addition of the 2 arrest-related variables, the predictive ability was modestly improved (c statistic=0.78).

Results of multinomial logistic regression are provided in Table 5. Compared with multivariable modeling, there was general consistency in the magnitude and direction of associations for NIS versus death or CPC-5 but not for NIS versus survival with significant neurological impairment (CPC-3 or -4). In particular, there were no factors that seemed to increase the odds of NIS and several of which had correlated with a decreased odds of NIS on multivariable analysis (ie, continuous infusion of vasopressors or dobutamine hypotension/hypoperfusion, malignancy at baseline, septicemia or renal insufficiency diagnosed during the index admission, and

age) no longer exhibited such an association. Nonetheless, a strong inverse relationship did persist for 7 variables including acute stroke or nonstroke CNS event within 4 hours of arrest, CNS depression or hepatic insufficiency at baseline, pacemaker use or assisted or mechanical ventilation before arrest, and black race.

Discussion

In this analysis of the NRCPR, 20% of patients with acute HF who suffered an in-hospital cardiac arrest were discharged alive, nearly 89% of whom were neurologically intact. After adjustment for important variables including cardiac monitoring before arrest, the presence of any ventricular fibrillation or pulseless ventricular tachycardia during the arrest and duration of the arrest event, 18 prearrest factors were found to be associated with NIS, 4 positively and 14 negatively. Response to these factors was relatively uniform, even among subgroups stratified by the presence or absence of potentially life-limiting, preexisting comorbidities. For a number of inversely associated factors, the nature of the response was also fairly robust, persisting whether outcome was evaluated as a dichotomous or polytomous occurrence.

Although establishment of a cause and effect relationship is not possible with our study design, our results provide compelling evidence that NIS may be more (or less) likely in the presence of specific, readily identifiable variables. Although our data did not enable derivation of a valid composite model, consideration of these variables in the prearrest period would help objectify the process of resuscitative goal setting and enhance the information on which patients and providers establish their preferences for (or against) do not resuscitate status. Although such decisions are inherently complex, our data provide a reasonable representation of factors that, if applied prospectively, could foster direction of resuscitative efforts toward those most likely to derive meaningful benefit.

Of the individual factors that were associated with an increased odds of NIS, the absence of therapeutic interventions and presence of arrhythmias before arrest are the most intuitive. Patients with acute HF who are not receiving continuous medication infusions and have no advanced device therapy or monitoring in place before arrest would presumably be less symptomatic and more stable from a hemodynamic perspective at baseline. This may in turn be reflective of better underlying cardiovascular reserve, which would increase the likelihood of recovery after a life-threatening cardiac event.²⁴ That arrhythmias were independently associated with an increased odds of NIS likely reflects their inherently treatable nature as a precipitant of cardiac arrest.

Diabetes mellitus and pulmonary artery catheter use were also positively associated with NIS, but the nature of these relationships is less clear. Previous research has demonstrated a neutral or negative effect of diabetes on outcome for the general in-hospital cardiac arrest population,^{24,25} and our results may be reflective of a specific interaction between diabetes mellitus and acute HF. Such an interaction may be mediated in part by underlying coronary artery disease, which has been shown to correlate with a decreased likelihood of death for diabetic patients with chronic HF.²⁶ Similarly, that we found

Table 4. Adjusted Association of Prearrest Variables With Neurologically Intact Survival Initially Without Then With Inclusion of Arrest Variables

Characteristic*	Adjusted for Prearrest Variables Only			Adjusted for Prearrest and Arrest Variables		
	OR	95% CI		OR	95% CI	
		Lower	Upper		Lower	Upper
Acute stroke	0.44	0.30	0.67	0.38	0.25	0.58
Continuous infusion—vasopressors	0.47	0.40	0.55	0.50	0.43	0.59
Malignancy	0.51	0.41	0.65	0.49	0.39	0.63
Hepatic insufficiency	0.62	0.49	0.77	0.59	0.46	0.75
Acute CNS event (nonstroke)	0.62	0.50	0.78	0.59	0.46	0.74
Hypotension/hypoperfusion	0.62	0.55	0.70	0.65	0.58	0.74
Septicemia	0.66	0.55	0.78	0.62	0.52	0.75
Assisted or mechanical ventilation	0.65	0.57	0.75	0.53	0.45	0.61
Baseline CNS depression	0.73	0.60	0.88	0.71	0.58	0.86
Black race	0.74	0.64	0.84	0.77	0.67	0.89
Pacemaker	0.83	0.72	0.97	0.85	0.72	1.00
Renal insufficiency	0.85	0.76	0.94	0.84	0.75	0.93
Continuous infusion—dobutamine	0.85	0.70	1.05	0.79	0.64	0.99
Female gender	0.89	0.80	0.98	0.92	0.83	1.02
Respiratory insufficiency	0.89	0.81	0.99	0.96	0.86	1.06
Age	0.98	0.98	0.99	0.98	0.98	0.98
No therapeutic interventions	1.09	0.97	1.22	1.14	1.01	1.28
Acute myocardial infarction	1.11	1.00	1.24	1.09	0.98	1.22
Diabetes mellitus	1.13	1.03	1.25	1.18	1.06	1.30
Arterial line	1.28	1.05	1.57	1.23	0.99	1.52
Pulmonary artery catheter	1.35	1.06	1.73	1.33	1.02	1.73
Arrhythmia	1.40	1.27	1.55	1.27	1.15	1.41
Cardiac monitor	1.69	1.46	1.97	1.48	1.26	1.73
Any VF or pVT	NA	NA	NA	1.68	1.52	1.86
Log [duration of event]	NA	NA	NA	0.41	0.39	0.44

VF, ventricular fibrillation; pVT, pulseless ventricular tachycardia.

*Only characteristics with statistically significant associations are provided.

a positive association between pulmonary artery catheter use and NIS was unanticipated and contradictory to existing data.^{27,28} Although this may signal confounding from an unidentified parameter, the potential benefit of goal-directed, hemodynamic management is an intriguing consideration.

Particularly strong inverse relationships existed for 8 variables including acute stroke or nonstroke CNS events, malignancy at baseline, continuous infusion of vasopressors, assisted or mechanical ventilation, septicemia, hepatic insufficiency, and hypotension/hypoperfusion, with each portending a 40% to 50% reduction in the odds of NIS when present. Factors such as malignancy, sepsis, and mechanical ventilation have been previously found to correlate with decreased rates of cardiopulmonary resuscitation survival for the general population,^{13,29,30} and their association may be reflective of underlying critical illness rather than a direct association with acute HF. A correlation between hypotension/hypoperfusion and poor outcome in acute HF, however, has been consistently demonstrated,^{5,6,9,31} and our finding to that effect is not surprising. That continuous infusion of vasopressors

(and, to a lesser degree, dobutamine) was independently associated with non-NIS, however, suggests that risk may be especially high for patients who require pharmacotherapeutic measures to maintain adequate perfusion pressure.³²

It is both interesting and concerning that we found black race to correlate with a 23% lower likelihood of NIS. Previous analysis of the NRCPR did report an association between black race and delayed time to defibrillation, and this may be a critical factor.²⁰ Recent data from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF), however, show that black patients admitted with acute HF receive equal if not better care and have a lower risk of in-hospital mortality when compared with whites.³³ Black patients with HF also tend to be younger with less ischemic and more hypertensive heart disease, which portends a better overall prognosis. How race or other related factors contribute to non-NIS in acute HF therefore is not clear, but given the tremendous disease burden in the black community, this relationship merits further exploration.

Table 5. Multinomial Logistic Regression Model*

Characteristic†	Cerebral Performance Category 1 or 2 vs 3 or 4			Cerebral Performance Category 1 or 2 vs Dead or 5		
	OR	95% CI		OR	95% CI	
		Lower	Upper		Lower	Upper
Acute stroke	0.17	0.09	0.31	0.41	0.27	0.62
Acute CNS event (nonstroke)	0.41	0.27	0.62	0.60	0.48	0.76
Baseline CNS depression	0.48	0.33	0.70	0.72	0.59	0.88
Hepatic insufficiency	0.61	0.37	0.99	0.59	0.46	0.75
Pacemaker	0.66	0.46	0.96	0.87	0.73	1.02
Assisted or mechanical ventilation	0.70	0.50	0.97	0.52	0.45	0.60
Black race	0.70	0.51	0.97	0.77	0.67	0.89
Pneumonia	0.71	0.52	0.97	0.92	0.80	1.07
Septicemia	0.76	0.51	1.13	0.62	0.51	0.74
Respiratory insufficiency	0.76	0.59	0.99	0.97	0.87	1.08
Continuous infusion—dobutamine	0.78	0.47	1.30	0.80	0.64	0.99
Log [duration of event]	0.83	0.74	0.94	0.40	0.37	0.42
Hypotension/hypoperfusion	0.85	0.63	1.14	0.65	0.57	0.73
Arrhythmia	0.89	0.69	1.15	1.29	1.16	1.44
Age	1.00	0.99	1.01	0.98	0.97	0.98
No therapeutic interventions	1.05	0.79	1.40	1.14	1.01	1.28
Cardiac monitor	1.09	0.74	1.61	1.50	1.28	1.76
Diabetes mellitus	1.10	0.90	1.42	1.18	1.06	1.31
Renal insufficiency	1.13	0.86	1.47	0.82	0.74	0.92
Pulmonary artery catheter	1.40	0.73	2.71	1.33	1.03	1.73
Continuous infusion—vasopressors	1.48	0.97	2.25	0.48	0.41	0.56
Any VF or pVT	1.56	1.21	2.01	1.70	1.53	1.88
Malignancy	1.60	0.76	3.36	0.47	0.37	0.61

VF, ventricular fibrillation; pVT, pulseless ventricular tachycardia.

*Data for comparison of cerebral performance category (CPC) 3 or 4 vs dead or 5 not displayed.

†Only characteristics with statistically significant associations are provided.

Several important limitations should be considered when interpreting our findings. First, as with other multicenter national registries, there is a possibility of data abstraction and entry errors. The potential for this, however, is greatly minimized by a rigorous and highly regulated process of data collection as well as the use of reabstraction methods. Second, because coding for a number of preexisting conditions is dependent on a documented diagnosis in the medical record rather than prospective collection of objective data elements, there is potential for misclassification bias. Although it is impossible to know the extent to which this may have occurred, the impact should be minimized by incorporation of a sizeable study sample obtained from a large number of institutions in a variety of geographic locations. Third, because participation in the NRCPR is voluntary, sampling bias may be present. The contributing centers account for ≈10% of all hospitals in the United States, and the quality of care/outcomes delivered at these institutions may differ from those who are not part of the NRCPR. Nonetheless, participating hospitals represent the entire spectrum with regard to important characteristics (size, teaching status, etc), and the patient characteristics of those in the

database are generally similar to existing studies. Last, our study was retrospective in nature and based on observational data compiled to evaluate cardiac arrest in a broad cross-section of patients rather than an acute HF-specific cohort. As such, we were neither able to incorporate a comparator group of patients with acute HF without cardiac arrest nor able to adjust for potentially important variables that can influence outcomes such as HF etiology (although we were able to control for the presence of acute or previous myocardial infarction) or severity of cardiac dysfunction. Moreover, the NRCPR does not collect data on whether HF was associated with preserved or reduced left ventricular function, which, as shown by previous studies such as OPTIMIZE-HF³⁴ and the Acute Decompensated Heart Failure Registry,³⁵ has critical bearing on in-hospital survival.

In conclusion, we identified 18 factors that were either positively or negatively associated with NIS for patients with acute HF and in-hospital cardiac arrest. Although the nature of the NRCPR precludes establishment of cause and effect, several factors exhibited a strong and robust inverse relationship with NIS. Consideration of these factors before cardiac arrest could improve the resuscitative decision-making pro-

cess and enhance resource utilization for those at risk of adverse outcome.

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CLINICAL PERSPECTIVE

Patients admitted to the hospital with acute heart failure are at high risk for cardiac arrest, yet data are surprisingly limited regarding factors that may be associated with neurologically intact survival. We sought to address this gap in knowledge by using a multisite national registry of in-hospital cardiac arrest. Among ≈13 000 cardiac arrest cases with acute heart failure, of whom 20% survived to discharge, we found neurologically intact survival to be associated with the presence or absence of specific, readily identifiable variables. An inverse relationship was particularly strong for several factors, including history of malignancy, concurrent sepsis or acute neurological events (stroke or nonstroke), and the use of mechanical ventilation or vasopressor therapy before arrest. A better understanding of these predictors of neurologically intact survival could facilitate the discussion of resuscitative preferences and enhance the information on which patients with acute heart failure base their decision making.

Factors Associated With Neurologically Intact Survival for Patients With Acute Heart Failure and In-Hospital Cardiac Arrest

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SUPPLEMENTAL MATERIAL

Supplemental Table

Appendix A: Operational Definitions

Pre-Existing Conditions

- Acute central nervous system (CNS) non-stroke event - decreased mental status, delirium, or coma not due to acute stroke within 4-hours up to time of the event.
- Acute stroke - documented diagnosis of an intracranial/intraventricular hemorrhage or thrombosis during index admission.
- Arrhythmia - any rhythm disturbance, excluding sinus tachycardia at any time during index admission prior to the event.
- Baseline depression in CNS function - evidence of a motor, cognitive, or functional baseline deficit at time of system entry.
- Prior history of heart failure - documented diagnosis of congestive heart failure prior to index admission.
- Diabetes mellitus - documented diagnosis of Type I or Type II diabetes mellitus.
- Hepatic insufficiency - total bilirubin > 2 mg/dL *and* AST > 2x normal or known cirrhosis.
- Hypotension/hypoperfusion - within 4-hours up to the time of the event, either systolic blood pressure (SBP) < 90 or mean arterial pressure (MAP) < 60 mmHg, vasopressor/inotropic requirement after volume expansion (except for dopamine \leq 3mcg/kg/min) or need for intra-aortic balloon pump.
- Metastatic or hematologic malignancy - any solid tissue malignancy with evidence of metastasis, or any blood borne malignancy.
- Metabolic/electrolyte abnormality - ANY of the following within 4-hours of the event:

- Sodium < 125 or > 150 mEq/L
- Potassium < 2.5 or > 6 mEq/L
- pH < 7.3 or > 7.5, arterial
- Lactate > 2.5 mmol/L
- Blood glucose < 60 mg/dL
- Acute myocardial infarction - documented diagnosis of myocardial ischemia, acute coronary syndrome or infarction this admission.
- Prior history of myocardial infarction - documented diagnosis of myocardial ischemia, acute coronary syndrome or infarction prior to this admission.
- Pneumonia - documented diagnosis of active pneumonia prior to event.
- Renal insufficiency - ongoing dialysis or extracorporeal filtration therapies or reatinine > 2 mg/dL within 24-hours up to the time of the event.
- Respiratory insufficiency - ANY of the following within 4-hours of the event:
 - PaO₂/FiO₂ ratio < 300
 - PaO₂ < 60 mm Hg
 - SaO₂ < 90
 - PaCO₂, EtCO₂ or TcCO₂ > 50 mm Hg
 - Spontaneous respiratory rate > 40/min or < 5/min
 - Requiring assisted ventilation (invasive or non-invasive)
- Septicemia - documented bloodstream infection prior to event.

Interventions In-Place

- Assisted or mechanical ventilation – non-invasive or invasive ventilator assisted airway support.

- Arterial line – intra-arterial blood pressure monitoring catheter.
- Pacemaker – use of transcutaneous, transvenous or epicardiac pacing device.
- Cardiac monitoring – continuous non-invasive cardiac rhythm monitoring.
- Central venous line – internal jugular, subclavian or femoral vein vascular access.
- Pulmonary artery (PA) catheter – invasive hemodynamic monitoring with Swan-Ganz catheter.
- Dialysis – hemodialysis, peritoneal dialysis, or continuous arteriovenous or veno-venous hemofiltration.
- Implantable cardioverter defibrillator (ICD) – pre-existing presence of device.
- Intra-aortic balloon pump (IABP) – use of internal balloon counterpulsation.
- Continuous infusion therapy – continuous intravenous treatment with ANY of the following:
 - Vasopressors (epinephrine, norepinephrine, phenylephrine or dopamine)
 - Dobutamine
 - Phosphodiesterase inhibitors (PDEI; amrinone or milrinone)
 - Lidocaine
 - Amiodarone
 - Procainamide
 - Nitroglycerin
 - Nitroprusside

