

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

Phillip D. Levy, MD, MPH; Hong Ye, MS; Scott Compton, PhD; Paul S. Chan, MD, MSc; Gregory Luke Larkin, MD; Robert D. Welch, MD, MS; for the American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators

**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  $\geq 65$  years.<sup>1</sup> 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.<sup>2-4</sup> For those patients who suffer acute decompensation, risk is also relatively high with in-hospital mortality estimates ranging from 1.8% to 8.9%.<sup>2,5,6</sup>

## Clinical Perspective on p 581

More than 80% of HF-related deaths occur among the elderly, the majority of which are due to sudden cardiac arrest.<sup>7</sup> 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<sup>2,6,8,9</sup> 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.<sup>10,11</sup> 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.<sup>12-14</sup> 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.<sup>15,16</sup>

Received January 7, 2009; accepted September 23, 2009.

From the Department of Emergency Medicine and the Cardiovascular Research Institute (P.D.L., R.W.), Wayne State University School of Medicine, Detroit, Mich; Department of Radiation Oncology (H.Y.), William Beaumont Hospital, Royal Oak, Mich; Department of Emergency Medicine (S.C.), University of Medicine and Dentistry, Newark, NJ; Mid America Heart Institute (P.S.C.), St. Luke' Health System, Kansas City, Mo; Department of Emergency Medicine (G.L.L.), Yale School of Medicine, New Haven, Conn.

The online-only Data Supplement is available at <http://circheartfailure.ahajournals.org/cgi/content/full/CIRCHEARTFAILURE.109.839829>.

Correspondence to Phillip D. Levy, MD, MPH, Department of Emergency Medicine, Wayne State University School of Medicine, 4201 St. Antoine, Detroit, MI 48201. E-mail [plevy@med.wayne.edu](mailto:plevy@med.wayne.edu)

© 2009 American Heart Association, Inc.

*Circ Heart Fail* is available at <http://circheartfailure.ahajournals.org>

DOI: 10.1161/CIRCHEARTFAILURE.108.828095

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.<sup>17</sup> 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.<sup>18</sup> 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.<sup>17,19</sup> 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.<sup>19</sup> 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,  $\geq 18$  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.<sup>19</sup> 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).<sup>19–21</sup> 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).<sup>13,14,19,21–23</sup> 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,

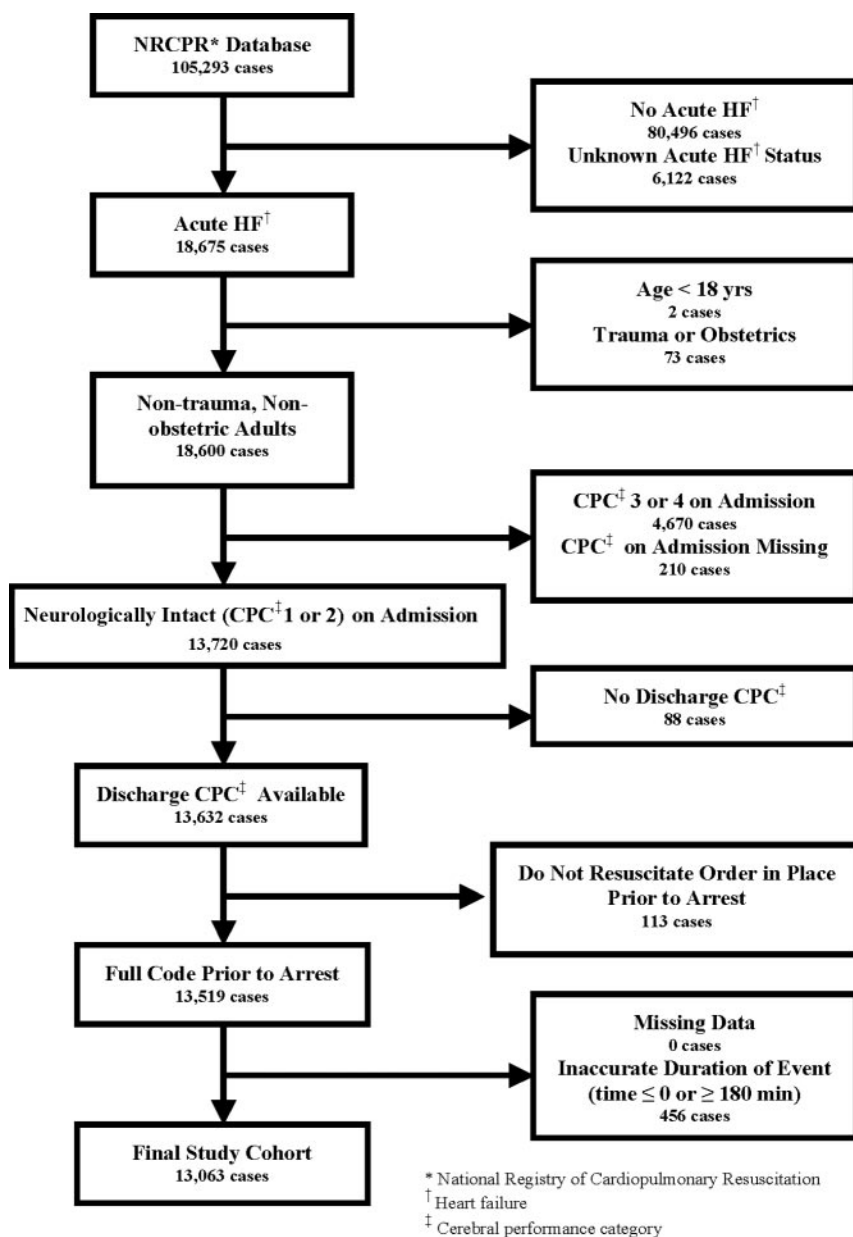


Figure 1. Study cohort derivation flow chart.

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 $\geq 4$ 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.

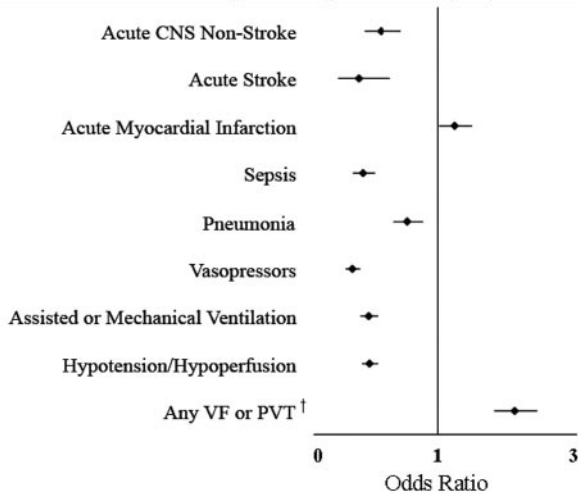
**Table 3. Characteristics and Their Association With Neurologically Intact Survival in Unadjusted Analysis**

| Characteristic                         | Neurologically Intact Survival (n=2307) | Nonneurologically Intact Survival (n=10 756) | Unadjusted Odds Ratios (95% CI) |
|--|---|--|---------------------------------|
| <b>Age, y</b>                          |   |  |                                 |
| 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)                |
| <b>Race, n (%)</b>                     |   |  |                                 |
| White                                  | 1762 (76.4)                             | 7776 (72.3)                                  |                                 |
| Black                                  | 343 (14.9)                              | 2030 (18.9)                                  |                                 |
| Other                                  | 202 (8.8)                               | 950 (8.8)                                    |                                 |
| <b>Residence, n (%)</b>                |   |  |                                 |
| Home                                   | 1857 (80.5)                             | 8539 (79.4)                                  | 1.07 (0.96–1.20)                |
| Nonhome*                               | 450 (19.5)                              | 2217 (20.6)                                  |                                 |
| <b>Preexisting conditions, n (%)</b>   |   |  |                                 |
| 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)                |
| <b>Interventions in-place, n (%)</b>   |   |  |                                 |
| 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)                |
| <b>Continuous infusions</b>            |   |  |                                 |
| 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)                |

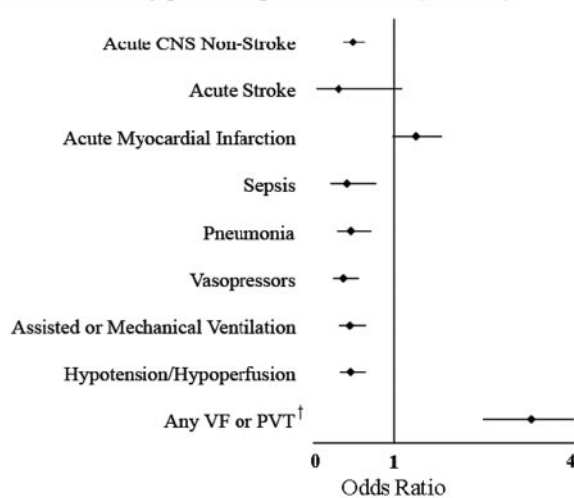
IQR indicates interquartile range.

\*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.

<sup>†</sup>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.<sup>24</sup> 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,<sup>24,25</sup> 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.<sup>26</sup> 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.<sup>27,28</sup> 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,<sup>13,29,30</sup> 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,<sup>5,6,9,31</sup> 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.<sup>32</sup>

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.<sup>20</sup> 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.<sup>33</sup> 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<br>1 or 2 vs 3 or 4 |        |       | Cerebral Performance Category<br>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-HF<sup>34</sup> and the Acute Decompensated Heart Failure Registry,<sup>35</sup> 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.

### Acknowledgments

We thank the American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators including the following members of the Adult Task Force and Scientific Advisory Board for their contributions to this manuscript: Tim Mader, MD (Tufts University); Karl B. Kern, MD (University of Arizona Medical Center); Sam Warren, MD (University of Washington); Graham Nichol, MD (University of Washington); Thomas Noel, MD (Virginia Commonwealth University Health System); Joseph P. Ornato, MD (Virginia Commonwealth University Health System); Mary Ann Peberdy, MD (Virginia Commonwealth University Health System); Romergryko Geocadin, MD (Johns Hopkins School of Medicine); Scott Braithwaite, MD (Yale University School of Medicine); Mary E. Mancini, RN, PhD (University of Texas at Arlington); Robert A. Berg, MD (University of Pennsylvania School of Medicine); Emilie Allen, BSN (Parkland Health and Hospital System); Kathy Duncan, RN (Institute for Healthcare Improvement); Vinay M. Nadkarni, MD (University of Pennsylvania School of Medicine); Gregory Luke Larkin, MD (Yale University School of Medicine); John Gosbee, MD (VA National Center for Patient-Safety); Greg Mears, MD (University of North Carolina); Elizabeth A. Hunt, MD (Johns Hopkins Simulation Center); Tanya Lane Truitt, RN, MS (NRCPR Consultant); William Kaye, MD (NRCPR Consultant); Melinda Smyth, MSN (NRCPR Consultant); Jerry Potts, PhD (American Heart Association); and Brian Eigel, PhD (American Heart Association). The American Heart Association National Registry of Cardiopulmonary Resuscitation investigators include P. Chan, E. Allen, R. Berg, S. Braithwaite, B. Eigel, R. Geocadin, E. Hunt, K. Kern, G. Larkin, T. Mader, M. Mancini, V. Nadkarni, G. Nichol, T. Noel, J. Ornato, M. Peberdy, J. Potts, T. Truitt, and S. Warren.

### Sources of Funding

None.

### Disclosures

None.

### References

- Rosamond W, Flegal K, Furie K, Go A, Greenland K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, Hong Y. Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117:e25–e146.
- Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *J Am Med Assoc*. 2003;290:2581–2587.
- Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KK, Murabito JM, Vasan RS. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med*. 2002;347:1397–1402.
- Roger VL, Weston SA, Redfield MM, Hellermann-Homan JP, Killian J, Yawn BP, Jacobsen SJ. Trends in heart failure incidence and survival in a community-based population. *J Am Med Assoc*. 2004;29:344–350.
- Gheorghiadu M, Abraham WT, Albert NM, Greenberg BH, O'Connor CM, She L, Stough WG, Yancy CW, Young JB, Fonarow GC. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. *J Am Med Assoc*. 2006;296:2217–2226.
- Fonarow GC, Adams KF Jr, Abraham WT, Yancy CW, Boscardin WJ. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. *J Am Med Assoc*. 2005;293:572–580.
- Mozaffarian D, Anker SD, Anand I, Linker DT, Sullivan MD, Cleland JG, Carson PE, Maggioni AP, Mann DL, Pitt B, Poole-Wilson PA, Levy WC. Prediction of mode of death in heart failure: the Seattle Heart Failure Model. *Circulation*. 2007;116:392–398.
- Levy WC, Mozaffarian D, Linker DT, Sutradhar SC, Anker SD, Cropp AB, Anand I, Maggioni A, Burton P, Sullivan MD, Pitt B, Poole-Wilson PA, Mann DL, Packer M. The Seattle Heart Failure Model: prediction of survival in heart failure. *Circulation*. 2006;113:1424–1433.
- Hsieh M, Auble TE, Yealy DM. Validation of the Acute Heart Failure Index. *Ann Emerg Med*. 2008;51:37–44.
- Krumholz HM, Phillips RS, Hamel MB, Teno JM, Bellamy P, Broste SK, Califf RM, Vidaillet H, Davis RB, Muhlbaier LH, Connors AF Jr, Lynn J, Goldman L. Resuscitation preferences among patients with severe congestive heart failure: results from the SUPPORT project. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Circulation*. 1998;98:648–655.
- Agard A, Hermeren G, Herlitz J. Should cardiopulmonary resuscitation be performed on patients with heart failure? The role of the patient in the decision-making process. *J Intern Med*. 2000;248:279–286.
- Brindley PG, Markland DM, Mayers I, Kutsogiannis DJ. Predictors of survival following in-hospital adult cardiopulmonary resuscitation. *CMAJ*. 2002;167:343–348.
- Cohn AC, Wilson WM, Yan B, Joshi SB, Heily M, Morley P, Maruff P, Grigg LE, Ajani AE. Analysis of clinical outcomes following in-hospital adult cardiac arrest. *Intern Med J*. 2004;34:398–402.
- Danciu SC, Klein L, Hosseini MM, Ibrahim L, Coyle BW, Kehoe RF. A predictive model for survival after in-hospital cardiopulmonary arrest. *Resuscitation*. 2004;62:35–42.
- Goodlin SJ, Hauptman PJ, Arnold R, Grady K, Hershberger RE, Kutner J, Masoudi F, Spertus J, Dracup K, Cleary JF, Medak R, Crispell K, Pina I, Stuart B, Whitney C, Rector T, Teno J, Renlund DG. Consensus statement: palliative and supportive care in advanced heart failure. *J Card Fail*. 2004;10:200–209.
- Kirkpatrick JN, Kim AY. Ethical issues in heart failure: overview of an emerging need. *Perspect Biol Med*. 2006;49:1–9.
- Peberdy MA, Kaye W, Ornato JP, Larkin GL, Nadkarni V, Mancini ME, Berg RA, Nichol G, Lane-Truitt T. Cardiopulmonary resuscitation of adults in the hospital: a report of 14720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. *Resuscitation*. 2003;58:297–308.
- Booth CM, Boone RH, Tomlinson G, Detsky AS. Is this patient dead, vegetative, or severely neurologically impaired? Assessing outcome for comatose survivors of cardiac arrest. *J Am Med Assoc*. 2004;291:870–879.
- Nadkarni VM, Larkin GL, Peberdy MA, Carey SM, Kaye W, Mancini ME, Nichol G, Lane-Truitt T, Potts J, Ornato JP, Berg RA. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *J Am Med Assoc*. 2006;295:50–57.
- Chan PS, Krumholz HM, Nichol G, Nallamothu BK. Delayed time to defibrillation after in-hospital cardiac arrest. *N Engl J Med*. 2008;358:9–17.
- Herlitz J, Bang A, Aune S, Ekstrom L, Lundstrom G, Holmberg S. Characteristics and outcome among patients suffering in-hospital cardiac arrest in monitored and non-monitored areas. *Resuscitation*. 2001;48:125–135.
- van Walraven C, Forster AJ, Parish DC, Dane FC, Chandra KM, Durham MD, Whaley C, Stiell I. Validation of a clinical decision aid to discontinue in-hospital cardiac arrest resuscitations. *J Am Med Assoc*. 2001;285:1602–1606.
- Nichol G, Stiell IG, Hebert P, Wells GA, Vandemheen K, Laupacis A. What is the quality of life for survivors of cardiac arrest? A prospective study. *Acad Emerg Med*. 1999;6:95–102.
- Mullner M, Sterz F, Behringer W, Schorkhuber W, Holzer M, Laggner AN. The influence of chronic prearrest health conditions on mortality and functional neurological recovery in cardiac arrest survivors. *Am J Med*. 1998;104:369–373.
- Rogove HJ, Safar P, Sutton-Tyrrell K, Abramson NS. Old age does not negate good cerebral outcome after cardiopulmonary resuscitation: analyses from the brain resuscitation clinical trials. The Brain Resuscitation Clinical Trial I and II Study Groups. *Crit Care Med*. 1995;23:18–25.
- From AM, Leibson CL, Bursi F, Redfield MM, Weston SA, Jacobsen SJ, Rodeheffer RJ, Roger VL. Diabetes in heart failure: prevalence and impact on outcome in the population. *Am J Med*. 2006;119:591–599.
- Shah MR, Hasselblad V, Stevenson LW, Binanay C, O'Connor CM, Sopko G, Califf RM. Impact of the pulmonary artery catheter in critically ill patients: meta-analysis of randomized clinical trials. *J Am Med Assoc*. 2005;294:1664–1670.

28. Binanay C, Califf RM, Hasselblad V, O'Connor CM, Shah MR, Sopko G, Stevenson LW, Francis GS, Leier CV, Miller LW. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *J Am Med Assoc.* 2005;294:1625–1633.
29. Bedell SE, Delbanco TL, Cook EF, Epstein FH. Survival after cardiopulmonary resuscitation in the hospital. *N Engl J Med.* 1983;309:569–576.
30. Ebell MH. Prearrest predictors of survival following in-hospital cardiopulmonary resuscitation: a meta-analysis. *J Fam Pract.* 1992;34:551–558.
31. Abraham WT, Fonarow GC, Albert NM, Stough WG, Gheorghide M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB. Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the OPTIMIZE-HF. *J Am Coll Cardiol.* 2008;52:347–356.
32. Abraham WT, Adams KF, Fonarow GC, Costanzo MR, Berkowitz RL, LeJemtel TH, Cheng ML, Wynne J. In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). *J Am Coll Cardiol.* 2005;46:57–64.
33. Yancy CW, Abraham WT, Albert NM, Clare R, Stough WG, Gheorghide M, Greenberg BH, O'Connor CM, She L, Sun JL, Young JB, Fonarow GC. Quality of care and outcomes for African Americans hospitalized with heart failure: findings from the OPTIMIZE-HF registry. *J Am Coll Cardiol.* 2008;51:1675–1684.
34. Fonarow GC, Stough WG, Abraham WT, Albert NM, Gheorghide M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF Registry. *J Am Coll Cardiol.* 2007;50:768–777.
35. Sweitzer NK, Lopatin M, Yancy CW, Mills RM, Stevenson LW. Comparison of clinical features and outcomes of patients hospitalized with heart failure and normal ejection fraction (> or =55%) versus those with mildly reduced (40% to 55%) and moderately to severely reduced (<40%) fractions. *Am J Cardiol.* 2008;101:1151–1156.

### 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

Phillip D. Levy, Hong Ye, Scott Compton, Paul S. Chan, Gregory Luke Larkin and Robert D. Welch

for the American Heart Association National Registry of Cardiopulmonary Resuscitation Investigators

*Circ Heart Fail.* 2009;2:572-581; originally published online September 28, 2009;  
doi: 10.1161/CIRCHEARTFAILURE.108.828095

*Circulation: Heart Failure* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2009 American Heart Association, Inc. All rights reserved.  
Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://circheartfailure.ahajournals.org/content/2/6/572>

Data Supplement (unedited) at:

<http://circheartfailure.ahajournals.org/content/suppl/2009/10/29/CIRCHEARTFAILURE.108.828095.DC1>

**Permissions:** Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation: Heart Failure* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the [Permissions and Rights Question and Answer](#) document.

**Reprints:** Information about reprints can be found online at:  
<http://www.lww.com/reprints>

**Subscriptions:** Information about subscribing to *Circulation: Heart Failure* is online at:  
<http://circheartfailure.ahajournals.org/subscriptions/>

**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 ≤ 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:
  - PaO<sub>2</sub>/FiO<sub>2</sub> ratio < 300
  - PaO<sub>2</sub> < 60 mm Hg
  - SaO<sub>2</sub> < 90
  - PaCO<sub>2</sub>, EtCO<sub>2</sub> or TcCO<sub>2</sub> > 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

