JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 77, NO. 4, 2021
© 2021 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

# Risk Stratification Among Survivors of Cardiac Arrest Considered for Coronary Angiography

Ahmed A. Harhash, MD,[a,b] Teresa L. May, DO,[c] Chiu-Hsieh Hsu, PhD,[d] Sachin Agarwal, MD,[e] David B. Seder, MD,[c] Michael R. Mooney, MD,[f] Nainesh Patel, MD,[g] John McPherson, MD,[h] Paul McMullan, MD,[i] Richard Riker, MD,[c] Eldar Soreide, MD, PhD,[j] Karen G. Hirsch, MD,[k] Pascal Stammet, MD, PhD,[l] Alison Dupont, MD,[m] Sten Rubertsson, MD, PhD,[n] Hans Friberg, MD, PhD,[o] Niklas Nielsen, MD, PhD,[o] Tanveer Rab, MD,[p] Karl B. Kern, MD[a]

## ABSTRACT

**BACKGROUND** The American College of Cardiology Interventional Council published consensus-based recommendations to help identify resuscitated cardiac arrest patients with unfavorable clinical features in whom invasive procedures are unlikely to improve survival.

**OBJECTIVES** This study sought to identify how many unfavorable features are required before prognosis is significantly worsened and which features are most impactful in predicting prognosis.

**METHODS** Using the INTCAR (International Cardiac Arrest Registry), the impact of each proposed "unfavorable feature" on survival to hospital discharge was individually analyzed. Logistic regression was performed to assess the association of such unfavorable features with poor outcomes.

**RESULTS** Seven unfavorable features (of 10 total) were captured in 2,508 patients successfully resuscitated after cardiac arrest (ongoing cardiopulmonary resuscitation and noncardiac etiology were exclusion criteria in our registry). Chronic kidney disease was used in lieu of end-stage renal disease. In total, 39% survived to hospital discharge. The odds ratio (OR) of survival to hospital discharge for each unfavorable feature was as follows: age >85 years OR: 0.30 (95% CI: 0.15 to 0.61), time-to-ROSC >30 min OR: 0.30 (95% CI: 0.23 to 0.39), nonshockable rhythm OR: 0.39 (95% CI: 0.29 to 0.54), no bystander cardiopulmonary resuscitation OR: 0.49 (95% CI: 0.38 to 0.64), lactate >7 mmol/l OR: 0.50 (95% CI: 0.40 to 0.63), unwitnessed arrest OR: 0.58 (95% CI: 0.44 to 0.78), pH <7.2 OR: 0.78 (95% CI: 0.63 to 0.98), and chronic kidney disease OR: 0.96 (95% CI: 0.70 to 1.33). The presence of any 3 or more unfavorable features predicted <40% survival. Presence of the 3 strongest risk factors (age >85 years, time-to-ROSC >30 min, and non-ventricular tachycardia/ventricular fibrillation) together or ≥6 unfavorable features predicted a ≤10% chance of survival to discharge.

**CONCLUSIONS** Patients successfully resuscitated from cardiac arrest with 6 or more unfavorable features have a poor long-term prognosis. Delaying or even forgoing invasive procedures in such patients is reasonable.
(J Am Coll Cardiol 2021;77:360–71) © 2021 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]University of Arizona Sarver Heart Center, Tucson, Arizona, USA; [b]University of Vermont, Burlington, Vermont, USA; [c]Maine Medical Center, Portland, Maine, USA; [d]University of Arizona College of Public Health, Tucson, Arizona, USA; [e]Columbia Univeristy, New York, New York, USA; [f]Minneapolis Heart Institute, Minneapolis, Minnesota, USA; [g]Lehigh Valley Medical Center, Lehigh, Pennsylvania, USA; [h]Vanderbilt University Medical Center, Nashville, Tennessee, USA; [i]St. Thomas Heart, Nashville, Tennessee, USA; [j]Stavanger University Hospital, Stavanger, Norway; [k]Stanford University, Stanford, California, USA; [l]National Fire and Rescue Corps, Luxembourg, Luxembourg; [m]Northside Hospital, Lawrenceville, Georgia, USA; [n]Uppsala University, Uppsala, Sweden; [o]Lund University, Helsingborg, Sweden; and the [p]Emory University School of Medicine, Atlanta, Georgia, USA.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received October 7, 2020; revised manuscript received November 12, 2020, accepted November 16, 2020.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2020.11.043

Cardiac arrest is associated with significant mortality. The current overall survival rate from out-of-hospital cardiac arrest (OHCA) is 10% (1). Acute myocardial infarction is a common cause of OHCA, with at least 1 culprit lesion demonstrated in more than one-half of cardiac arrest survivors (2). Even among patients initially resuscitated, the survival to hospital discharge rate has previously been disappointing at approximately 25% (3). Recognition that the majority of patients (75%) initially achieving return of spontaneous circulation were dying in the hospital ushered in a new era of aggressive post-resuscitation care including targeted temperature management (TTM) and coronary angiography (CAG) with percutaneous coronary intervention (PCI), when appropriate (4). Improved post-cardiac arrest care and invasive procedures have doubled the survival to hospital discharge rate to 50% (5,6). However, the presence of certain unfavorable features post-resuscitation reduces the likelihood of good outcome to a very low level.

SEE PAGE 372

Accordingly, the American College of Cardiology (ACC) Interventional Council published a treatment algorithm in 2015 for triaging comatose cardiac arrest survivors for emergent cardiac catheterization laboratory activation using 10 unfavorable resuscitation features, determined by consensus. These features included unwitnessed arrest, initial rhythm non-ventricular fibrillation (VF), no bystander cardiopulmonary resuscitation (CPR), >30 min from collapse to return of spontaneous circulation (time-to-ROSC), ongoing CPR, pH <7.2, lactate >7 mmol/l, age >85 years, end-stage renal disease, and noncardiac etiology (7). It was suggested that the presence of "multiple unfavorable features" could predict poor outcome with or without advanced cardiac care. The original algorithm was designed to help identify those with a low likelihood of survival where further treatments may not add meaningful value, allowing providers to weigh the risks and benefits before proceeding with invasive management. However, neither the ranking importance of such risk factors nor the threshold number of risk factors for potentially limiting the benefit from invasive intervention has been previously described.

The ACC management algorithm has not been subsequently evaluated in a large cohort of cardiac arrest survivors. For the practicing interventionalist and intensivist, it remains unclear which individual features carry the worst prognosis, or how many unfavorable features should be present before taking a conservative approach to coronary interventions in the post-resuscitated population.

We retrospectively applied the proposed triage algorithm for post-resuscitation coronary angiography in the large INTCAR (International Cardiac Arrest Registry). Our goal was to examine whether the unfavorable features identified by the ACC post-resuscitation triage algorithm are equally associated with unfavorable outcome, or if some might be more important prognosticators than others. We also developed a prediction tool to assist in early triage regarding the utility of urgent coronary angiography post cardiac arrest.

**ABBREVIATIONS AND ACRONYMS**

**CKD** = chronic kidney disease

**CPC** = cerebral performance category

**ESRD** = end-stage renal disease

**OHCA** = out-of-hospital cardiac arrest

**PCI** = percutaneous coronary intervention

**ROSC** = return of spontaneous circulation

**STE** = ST-segment elevation

**VF** = ventricular fibrillation

**VT** = ventricular tachycardia

## METHODS

We used the INTCAR 2.0 dataset from 2007 to 2017. INTCAR 2.0 is a voluntary hospital-based registry of consecutive cardiac arrest patients (both in-hospital and out-of-hospital) admitted to large volume cardiac arrest centers in the United States and Northern Europe. The registry is deidentified and requires local ethics review board approval. Deidentified data are prospectively and retrospectively entered into the online server; quality is locally maintained and is the responsibility of the local PI. Within the registry, data are routinely evaluated for internal consistency and validity, and removed if inconsistencies cannot be reconciled. The INTCAR 2.0 database (introduced in 2011 as a revision and update to the original dataset) reflects more current practices than the 1.0 version (2006 to 2011), and is a better reflection of current standards of post-resuscitation care. It is also equally representative of European and U.S. patients, making it a truly international sample. Not all centers participated during the entire time period. Many centers contributed patients during a part of the data collection period, but discontinued data entry when they could no longer meet the participation criterion of entering all consecutive patients into the registry (i.e., they began enrolling such patients in randomized clinical trials, such as the TTM trial [8]). Some centers joined INTCAR toward the end of our study period (2007 to 2017).

This database contains the characteristics and outcomes of post-resuscitation cardiac arrest care. This database is unique, consisting of comatose individuals successfully resuscitated from cardiac arrest and their post-arrest treatments and outcomes. It consists of 143 datapoints including demographic characteristics, pre-arrest conditions, resuscitation characteristics, post-resuscitation therapies (defibrillation, targeted temperature management, coronary angiography, revascularization), and outcomes (survival to hospital discharge, neurological recovery, delayed functional outcome after hospital discharge). In total, 7 of the 10 factors in the ACC treatment algorithm (7) were available in the INTCAR database. Both ongoing CPR efforts and noncardiac causes of cardiac arrest were exclusion criteria for the INTCAR registry; they were hence not included in the database and could not be evaluated in this analysis (9–13). End-stage renal disease (ESRD) status was not included in the INTCAR registry, but chronic kidney disease (CKD) was included, so it was used as the eighth factor in lieu of ESRD for the analysis. The Institutional Review Board of each institution participating in the INTCAR registry approved data collection and participation, and the INTCAR steering committee approved this investigator-initiated registry-based project. All patient data were deidentified on entry. The study was reviewed by the Institutional Review Board at the University of Arizona, and given the observational nature of the study and the de-identification of subjects' data, approval was granted. Data analysis was performed at the University of Arizona.

The association of each unfavorable feature on survival to hospital discharge was individually analyzed (adjusted for other identified features, sex, pre-arrest conditions, and therapeutic interventions). Combinations of such features for predicting a hospital discharge survival rate of 40% (the INTCAR registry's average for those successfully resuscitated) and for a 10% discharge survival rate (a marked reduction from the expected 40% rate) were examined. The primary objective was to assess the association of such unfavorable features, independently and in various combinations, on survival to hospital discharge. Survival with good neurological status was a secondary endpoint (neurological status was assessed using the cerebral performance category [CPC]). A good neurological outcome was defined as a CPC score of 1 (normal) or 2 (mild or moderate functional impairment, but independent), and a poor neurological outcome was defined as a CPC score of 3 to 5, where CPC 3 indicates conscious with severe neurological disability and dependent, CPC 4 indicates coma or vegetative state, and CPC 5 indicates dead.

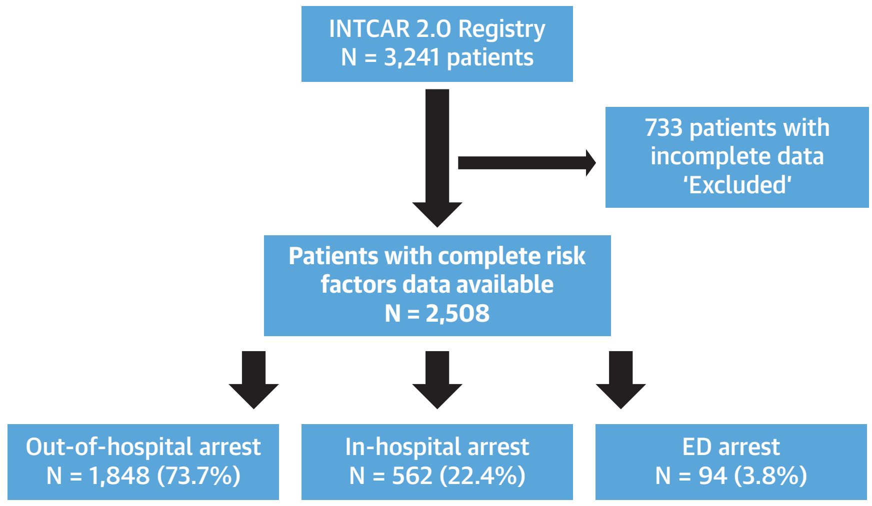
All patients 18 years of age or older who survived to admission to the hospital in a comatose state after cardiac arrest were included in the registry. Most patients included in the analysis were treated with target temperature management at a target core body temperature of 32°C to 34°C maintained for 24 h after return of spontaneous circulation.

Following the ACC management algorithm, patients were subsequently divided into 2 groups by their post-resuscitation electrocardiographic findings of ST-segment elevation (STE) or no STE.

**STATISTICAL ANALYSIS.** Patients surviving cardiac arrest, some but not all undergoing coronary angiography, were included, and were then subdivided into 2 groups (STE and no STE) according to their post-resuscitation ECG. The characteristics of these 2 groups were described by presenting frequencies, percentages for categorical variables, and mean ± SD for continuous variables. Fisher exact testing and 2-independent sample Student's *t*-testing with unequal variances were performed to compare categorical and continuous outcomes, respectively. Impact of individual unfavorable resuscitation feature was examined in an unadjusted fashion and was adjusted to the remaining 7 identified risk factors, sex, pre-arrest status (comorbidities, baseline CPC status), and delivered therapeutic interventions (defibrillation, coronary angiography, and revascularization). Univariate and multivariate logistic regression analyses were used to identify the significance of each unfavorable criterion on the above-mentioned outcome measures. Odds ratio and concordance statistic were reported to evaluate the association of each factor with survival to hospital discharge.

To further enhance the applicability of our findings and create a simplified tool to assist emergency personnel in triaging post-cardiac arrest survivors, we developed a prediction model for discharge survival based on the 8 identified unfavorable features among our cohort through the use of univariate and multivariate logistic regression. We then calculated the impact of multiple combinations of features to reliably predict a pre-determined survival threshold. We tested 2 different thresholds: a 40% likelihood of survival to hospital discharge as this marks the expected average survival to discharge of patients initially achieving return of spontaneous circulation, and a 10% likelihood of survival to hospital discharge, which reflects a dramatic reduction of expected survival to discharge for this patient population. Finally, we have conducted internal validation of our dataset based on 500 bootstrap samples and generated the calibration plot, as well as comparing the observed risk with the predicted risk. All statistical tests were 2-sided, and the significance level was set at 5%. All analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, North Carolina).

**FIGURE 1** Flow Diagram of the Study Population From the INTCAR 2.0 Registry




Flow diagram demonstrating the stepwise process for selecting the study cohort among cardiac arrest survivors enrolled in INTCAR 2.0 registry. INTCAR 2.0 consisted of 3,241 patients; 733 patients were excluded for missing details regarding the presence of unfavorable features, and the remaining 2,508 were included as the study cohort. Patients were then divided based on the cardiac arrest site, with 1,848 (74%) who experienced cardiac arrest out of the hospital, 562 (22%) in hospital, and 94 (4%) in the emergency department.
ED = emergency department; INTCAR = International Cardiac Arrest Registry.

## RESULTS

**BASELINE CHARACTERISTICS.** The INTCAR 2.0 database consists of 3,241 post-cardiac arrest patients from 2007 to 2017. A total of 733 patients were missing data regarding the 8 risk factors of interest and were excluded (Figure 1). A final total of 2,508 comatose post-cardiac arrest patients were therefore analyzed for this study, including 1,679 (67%) men, 1,848 (73.7%) with OHCA, 1,027 (41%) with ventricular fibrillation cardiac arrest, and 2,442 (84%) who received TTM. In total, 39% of these successfully resuscitated CA patients survived to hospital discharge. The unfavorable features were identified among these patients. A total of 20% (n = 504) had an unwitnessed arrest, 55% (n = 1,373) had a nonshockable initial cardiac arrest rhythm, 25% (n = 621) had no bystander CPR, and 27% (n = 671) had >30 min to ROSC, while 48% (n = 1,205) had an initial pH <7.2, 45% (n = 1,124) had a lactate >7 mmol/l, 4% (n = 98) were >85 years of age, and 14% (n = 363) had a history of CKD.

Post-resuscitation electrocardiography found 455 patients (19%) with STE. Coronary angiography was performed in 1,022 (43%) patients, and 555 (23%) underwent revascularization (PCI in 519 [21%] and coronary artery bypass surgery in 44 [2%]). Survival to hospital discharge was achieved in 976 (39%), while good neurological recovery (CPC 1 or 2) at hospital discharge was seen in 756 (77%) of survivors. Baseline demographics and resuscitation characteristics of the whole cohort are shown in Table 1.

**IMPACT OF EACH UNFAVORABLE FEATURE ON SURVIVAL TO HOSPITAL DISCHARGE.** The presence of any of the 8 unfavorable features post-ROSC predicted survival to hospital discharge when evaluated individually. When the evaluation was adjusted for the other risk factors, all, except CKD, remained strong predictors of decreased survival. The association of each feature (adjusted for the other risk features and delivered therapies) with survival to hospital discharge, from most predictive to least predictive, is illustrated in Figure 2A. Examining the association of such features on survival with favorable neurological outcome (CPC 1 or 2) confirmed similar findings with the exception of pH (Figure 2B).

**FINDING THE "TIPPING POINT": PREDICTION MODEL FOR HOSPITAL DISCHARGE SURVIVAL BASED ON THE 8 IDENTIFIED RISK FACTORS.** Time-to-ROSC >30 min, age >85 years, and non-ventricular tachycardia (VT)/VF presenting rhythm were the strongest negative predictors for survival to hospital discharge (Central Illustration). CKD was the only feature not predictive of worse outcome. When we used the model for combining the different unfavorable features to predict a <40% chance of survival to discharge, multiple combinations of 2 features still yielded a survival rate >40%. However, the presence

**TABLE 1 Summary of All Patient Characteristics (n = 2,508*)**

| | |
|---|---|
| Age, yrs | 62.1 ± 15.7 |
| >85 yrs | 98 (3.9) |
| Male | 1,679 (67.0) |
| OHCA | 1,848 (73.7) |
| Time-to-ROSC, min | 25 ± 19 |
| >30 min | 671 (26.7) |
| Lactate, mmol/l | 7.4 ± 6.5 |
| >7 mmol/l | 1,124 (44.8) |
| pH | 7.2 ± 0.2 |
| <7.2 | 1,205 (48.0) |
| Pre-arrest diseases | |
| Previously healthy | 423 (16.9) |
| CAD | 446 (17.8) |
| CHF | 478 (19.1) |
| Arrhythmia | 402 (16.0) |
| CKD | 363 (14.5) |
| IDDM | 314 (12.5) |
| Liver disease | 83 (3.3) |
| CVD | 252 (10.0) |
| PVD | 204 (8.1) |
| COPD | 426 (17.0) |
| Obese | 281 (11.2) |
| NIDDM | 359 (14.3) |
| Hypertension | 1,194 (47.6) |
| Cognitive impairment | 133 (5.3) |
| Solid tumor | 210 (8.4) |
| Malignancy | 246 (9.8) |
| Neurological disease | 373 (14.9) |
| Pre-arrest CPC | 2,448 |
| 1 | 2,029 (82.9) |
| 2 | 259 (10.6) |
| 3 | 156 (6.4) |
| 4 | 4 (0.2) |
| Witnessed arrest | 2,004 (79.9) |
| Bystander CPR | 1,887 (75.2) |
| Initial rhythm | |
| VT/VF | 1,027 (41.0) |
| PEA/asystole | 1,373 (54.7) |
| Unknown | 108 (4.3) |
| STE | 455/2,350 (19.4) |
| Treatments | |
| Defibrillation | 1,294/2,463 (52.5) |
| TTM used | 2,508/2,442 (84.3) |
| CAG | 1,022/2,365 (43.2) |
| PCI | 519/2,420 (21.5) |
| CABG | 44/2,357 (1.9) |
| Revascularization (PCI or CABG) | 555/2,431 (22.8) |
| Outcome | |
| Discharge survival | 976/2,485 (39.3) |
| Discharge CPC 1 or 2 of survivors | 756/2,485 (30.4) |

Values are mean ± SD, n (%), n, or n/N (%). *Excluded patients with missing data for the 8 identified risk factors.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CAG = coronary angiography; CHF = congestive heart failure; CKD = chronic kidney disease; COPD; chronic obstructive pulmonary disease; CPC = cerebral performance category; CPR = cardiopulmonary resuscitation; CVD = cerebral vascular disease; IDDM = insulin-dependent diabetes; NIDDM = noninsulin-dependent diabetes; OHCA = out-of-hospital cardiac arrest; PCI = percutaneous coronary intervention; PEA = pulseless electrical activity; PVD = peripheral vascular disease; ROSC = return of spontaneous circulation; STE = ST-segment elevation; TTM = target temperature management; VT/VF = ventricular tachycardia/ventricular fibrillation.

of any 3 unfavorable features reliably predicted survival <40%, that is, less than the expected survival rate for patients initially resuscitated. The same steps were taken to predict a 10% survival (markedly worse than the expected survival). Interestingly, the presence of the 3 most unfavorable features (age >85 years, time-to-ROSC >30 min, and non-VT/VF initial cardiac arrest rhythm) alone predicted survival of only 7%. However, to simplify the model we calculated all possible combinations of features and the presence of almost any 6 features (27 of 28 combinations), or the presence of any 7 features reliably predicted survival <10% (Figure 3, Tables 2 and 3, Supplemental Table 1).

On internal validation, the concordance statistic is 0.783 based on the original sample. The correction (i.e., optimism) derived from the internal validation is 0.002. This indicates that the corrected concordance statistic is 0.781, which is very similar to the original concordance statistic.

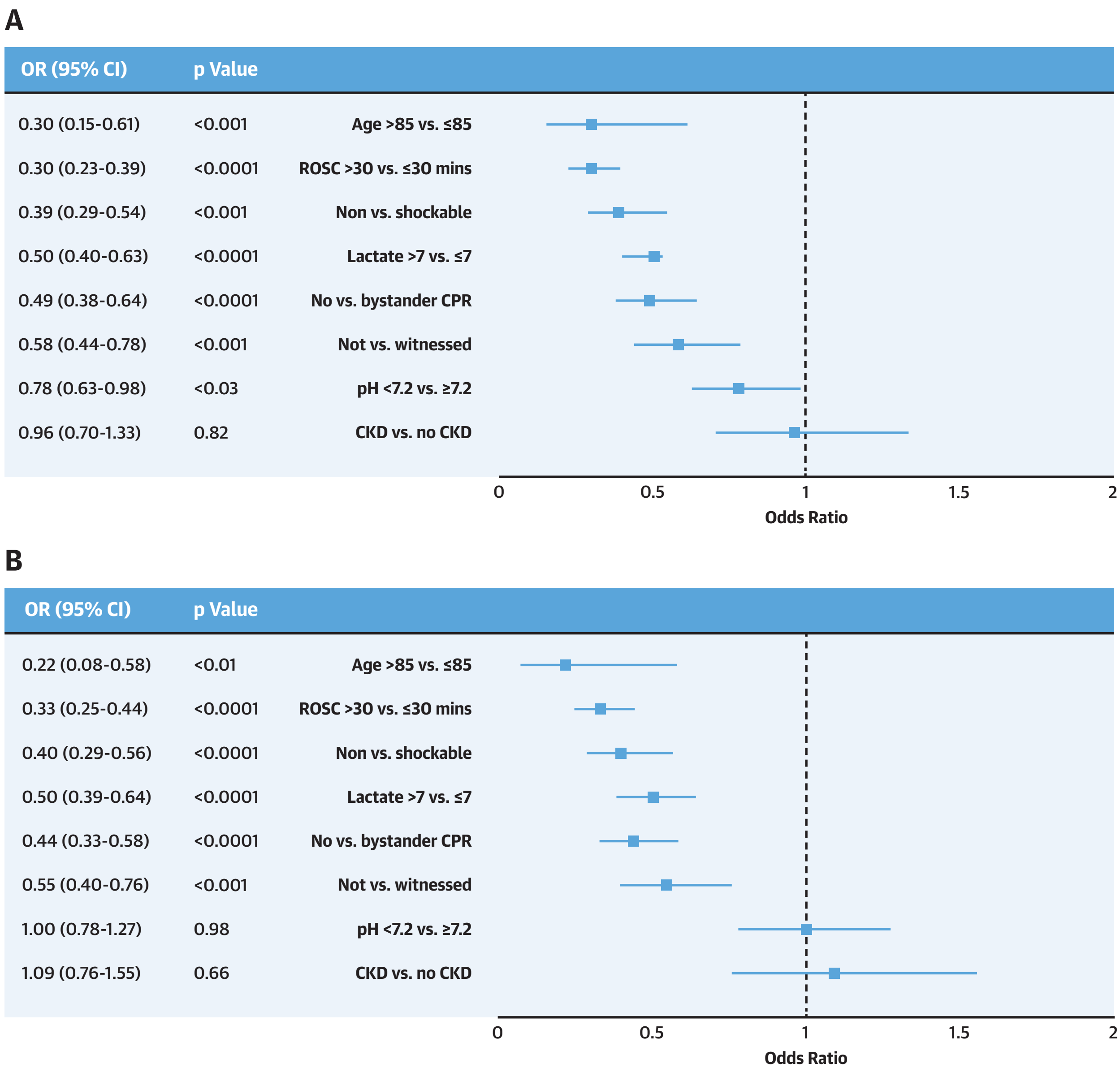
**STE VERSUS NO STE.** The STE group had more male patients compared with no STE (362 [80%] vs. 1,212 [64%]). There was no difference in average age for those with STE versus those without STE. More STE survivors were previously healthy compared with those without STE (127 [28%] vs. 273 [14%]), and STE patients had better functional status prior to cardiac arrest. STE survivors had less cardiac and noncardiac comorbidities. The STE group experienced more witnessed arrest (394 [87%] vs. 1,490 [79%]), and VT/VF on presentation (320 [70%] vs. 660 [35%]). Regarding delivered therapies, the STE group had more therapeutic interventions, including defibrillation, TTM, coronary angiography, and revascularization. The STE cohort had significantly greater survival to hospital discharge compared with those with no STE. Table 4 details the demographic, therapies, and outcome differences based on the presence or absence of STE.

Examining the association of these features with outcome after dividing the cohort based on the presence or absence of STE demonstrated similar findings where time-to-ROSC >30 min, age >85 years, and non-VT/VF again were the strongest predictors for poor outcome, in both groups. However, given the small sample size, 1 risk feature (age >85 years) did not reach statistical significance despite a very strong trend toward adverse outcome. These data are shown in Supplemental Figures 1A, 1B, 2A, and 2B.

## DISCUSSION

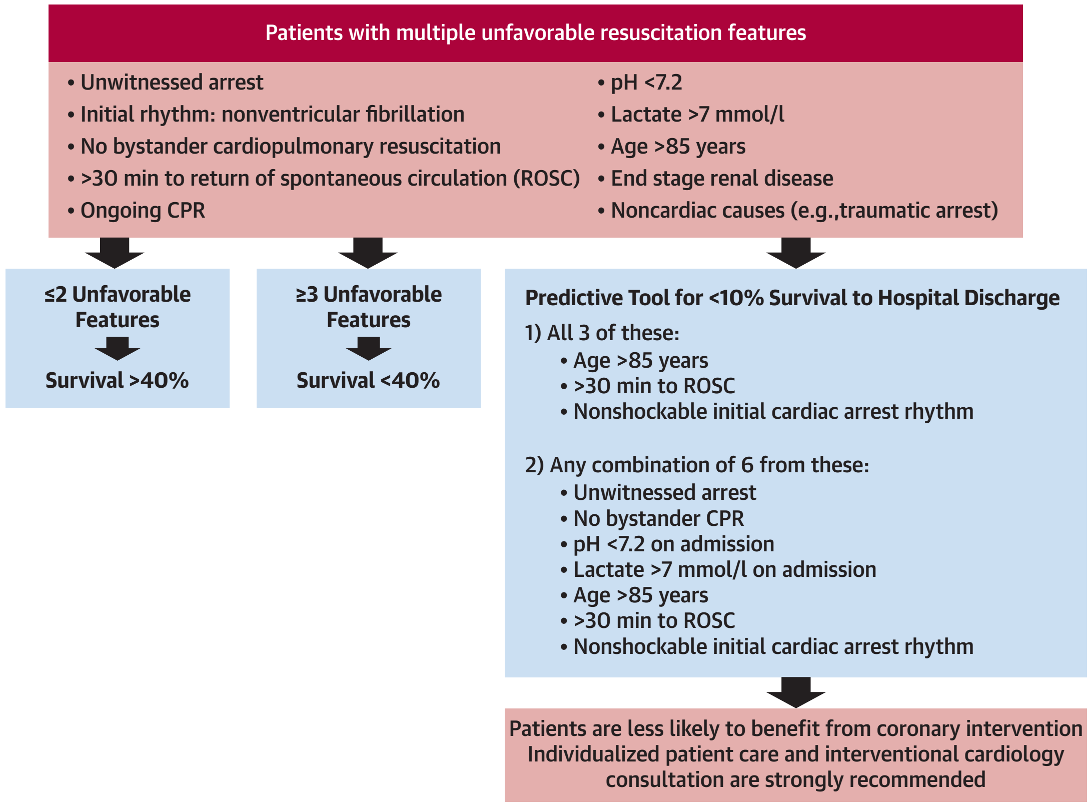
The INTCAR 2.0 dataset contained 7 of the 10 identified unfavorable features proposed for cardiac arrest triage purposes by the American College of

**FIGURE 2** **Importance of Each Unfavorable Feature on Survival to Hospital Discharge and Favorable Neurological Function at Discharge**




Forest plot demonstrating the impact of each unfavorable resuscitation feature on **(A)** hospital discharge survival, and **(B)** survival with good neurological recovery. Each unfavorable feature was examined in an unadjusted fashion and adjusted to the remaining 7 identified risk features; further adjustment was made for sex, pre-arrest status (comorbidities, baseline CPC status), and delivered therapeutic interventions (defibrillation, coronary angiography, and revascularization). Univariate and multivariate logistic regression analyses were used to identify the significance of each unfavorable feature on both outcomes measured. Odds ratios were reported to evaluate the association of each factor with survival to hospital discharge survival **(A)** and survival with good neurological recovery **(B)**. There was a strong association between almost all unfavorable features (except CKD, which was adapted in lieu of end-stage renal disease). Age >85 years, time-to-ROSC >30 min, and nonshockable presenting rhythms were the strongest predictors for poor survival to hospital discharge and for poor survival with good neurological recovery. CKD = chronic kidney disease; CI = confidence interval; CPC = cerebral performance category; CPR = cardiopulmonary resuscitation; OR = odds ratio.

**CENTRAL ILLUSTRATION** Simplified Tool for Predicting <10% and <40% Survival to Hospital Discharge in Successfully Resuscitated Cardiac Arrest Patients



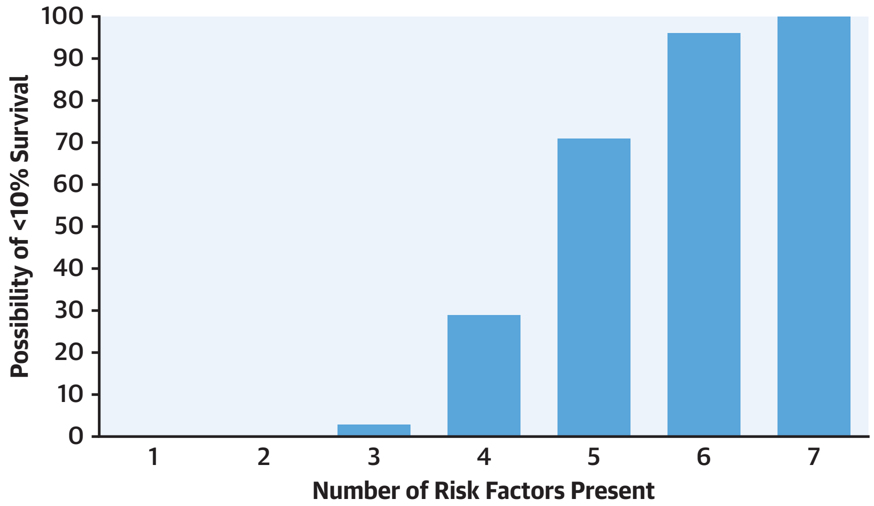

**Harhash, A.A. et al. J Am Coll Cardiol. 2021;77(4):360–71.**

The 10 unfavorable features for predicting poor outcome after initial resuscitation from out-of-hospital cardiac arrest (Adapted from Rab et al. [7], with permission). Triaging resuscitated cardiac arrest survivors based on the presence of unfavorable features will yield 3 possibilities: 1) if <2 unfavorable features are present, the chance of hospital discharge survival is >40%; 2) if any 3 or more unfavorable features present, the chance of hospital discharge survival is <40%; and 3) if any 6 of the listed features, or a combination of the 3 strongest unfavorable features (age >85 years, time-to-ROSC >30 min, and nonshockable presenting rhythm) is present, chance of hospital discharge survival is <10%. Such patients may be poor candidates for emergent invasive cardiovascular procedures. CPR = cardiopulmonary resuscitation; ROSC = return of spontaneous circulation.

Cardiology's Interventional Council (7). We attempted to use CKD as a substitute for ESRD, the eighth unfavorable feature. In total, 7 of these 8 features were associated in the univariate analysis with outcome. In the multivariable predictive model, we found age >85 years, time-to-ROSC >30 min, and non-VT/VF presenting rhythm were the strongest independent predictors of in-hospital mortality post-cardiac arrest, whereas CKD (our surrogate for end-stage renal disease) was not associated with worse outcomes. These findings were consistent after dividing the registry cohort based on the presence or absence of STE. The presence of age >85 years, time-to-ROSC >30 min, and an initial nonshockable rhythm predicted survival of <10%. We incorporated the other ACC Interventional Council factors, and any 6 or more unfavorable features also predicted <10% survival to discharge—a potential line beyond which performing invasive management strategies in such patients might be considered unproductive or even futile (Figure 3).

A total of 6 or more unfavorable features is associated with a 95% possibility of a very poor outcome (<10% survival to discharge) (Central Illustration). Even 5 or more features results in a 70% possibility of a <10% survival to discharge rate (Figure 3). Accordingly, the majority (>70%) of such initially resuscitated patients with 5 or more of the 10 unfavorable

**FIGURE 3** **Likelihood of Very Poor (<10%) Survival to Hospital Discharge Among Cardiac Arrest Survivors With Increasing Unfavorable Features Post-Resuscitation**




The chance of very poor (<10%) survival to hospital discharge increases with each additional unfavorable feature a patient accumulates, regardless of what the feature was. This prediction model for discharge survival based on the 8 identified unfavorable features among our cohort through the use of univariate and multivariate logistic regression. All patients presenting with only 1 or 2 features had survival >10%. Presence of only 1 combination of 3 unfavorable features predicted survival <10%. In the presence of 4 of such features the risk of <10% survival is 30%, with 5 features the risk is 75%, and with 6 or more the risk becomes 97% to 100%. This simplified graph did not account for the specific features present and suggested the "tipping point" for very poor survival appears to be 6 or more unfavorable features.

features have an expected survival to discharge rate of <10%. Two of the original 10 unfavorable features were not captured in the INTCAR 2.0 database, namely "ongoing CPR at hospital arrival" and "noncardiac etiology such as trauma for the cardiac arrest." Both of these features are known to be very strongly associated with poor long-term outcomes with survival to hospital rates <3% (14,15).

This study validates and refines the recommendations and algorithm regarding multiple unfavorable risk features previously described by the ACC Interventional Council among cardiac arrest survivors (7). Among more than 2,500 post-cardiac arrest survivors with arrests of presumed cardiac etiology in the INTCAR registry, we found significant demographic differences between those presenting with STE versus no STE. Survivors with STE were overall younger, were healthier, had less comorbidities, and were more likely to be functionally intact before the cardiac arrest. Also, the majority of STE survivors presented with shockable rhythms and underwent established therapeutic interventions (defibrillation, TTM, CAG, and revascularization). Most importantly, survival to hospital discharge was significantly better among STE survivors, and among those who survived, more patients had better neurological recovery compared with those with no STE. However, we found no difference in the number of unfavorable features associated with a very poor outcome whether the patient had STE or not.

We believe our findings provide an important tool helping the emergency responders, ED physicians, interventional cardiologists, and others caring for post-cardiac arrest survivors to determine who might benefit from urgent angiography, and who are not good candidates for such invasive therapies. Such

**TABLE 2** **Regression Model for Discharge Survival Based on the 8 Identified Risk Factors**

| Risk Factor | Coefficient ± SE | p Value |
|---|---|---|
| Intercept | 1.35 ± 0.09 | <0.0001 |
| Age >85 yrs | −1.39 ± 0.32 | <0.0001 |
| pH <7.2 | −0.28 ± 0.10 | <0.01 |
| Lactate >7 mmol/l | −0.65 ± 0.10 | <0.0001 |
| Not witnessed | −0.55 ± 0.13 | <0.0001 |
| No bystander CPR | −0.61 ± 0.12 | <0.0001 |
| Nonshockable | −1.45 ± 0.09 | <0.0001 |
| Time-to-ROSC >30 min | −1.12 ± 0.12 | <0.0001 |
| CKD | −0.26 ± 0.14 | 0.06 |

Abbreviations as in Table 1.

**TABLE 3 Predicted Discharge Survival Probability Based on the Model in Table 2***

| | Predicted Discharge Survival Probability, % (95% CI) |
|---|---|
| 1 risk factor | |
| Age >85 yrs | 49.0 (33.5–64.7) |
| pH <7.2 | 74.5 (69.8–78.7) |
| Lactate >7 mmol/l | 66.9 (61.5–71.9) |
| Not witnessed | 69.1 (62.5–75.1) |
| No bystander CPR | 67.8 (62.0–73.1) |
| Nonshockable | 47.7 (43.3–52.2) |
| Time-to-ROSC >30 min | 55.9 (49.4–62.1) |
| CKD | 74.9 (68.9–80.1) |
| 2 risk factors <40% | |
| Age >85 yrs + nonshockable | 18.5 (10.6–30.1) |
| Time-to-ROSC >30 min + nonshockable | 23.0 (18.3–28.4) |
| Age >85 yrs + time-to-ROSC >30 mins | 23.9 (13.8–38.2) |
| Lactate >7 mmol/l + nonshockable | 32.2 (27.4–37.5) |
| No bystander CPR + nonshockable | 33.1 (27.6–39.0) |
| Age >85 yrs + lactate >7 mmol/l | 33.3 (20.5–49.3) |
| Age >85 yrs + no bystander CPR | 34.3 (21.1–50.4) |
| Not witnessed + nonshockable | 34.5 (28.3–41.2) |
| Age >85 yrs + not witnessed | 35.7 (21.8–52.5) |
| Time-to-ROSC >30 yrs + lactate >7 mmol/l | 39.7 (33.2–46.7) |
| 3 risk factors <40% | |
| Any 3 risk factor combinations with sum of the coefficients <−1.76, excluding intercept | |

*$Pr(\text{discharge survival}) = \frac{\exp(1.3553 - 1.3937 \times (Age > 85) - 0.2820 \times (pH < 7.2) - 0.6527 \times (Lactate > 7) - 0.5496 \times Not\ Witnessed - 0.6128 \times No\ Bystander\ CPR - 1.4473 \times Nonshockable - 1.1191 \times (ROSC > 30) - 0.2629 \times CKD)}{1 + \exp(1.3553 - 1.3937 \times (Age > 85) - 0.2820 \times (pH < 7.2) - 0.6527 \times (Lactate > 7) - 0.5496 \times Not\ Witnessed - 0.6128 \times No\ Bystander\ CPR - 1.4473 \times Nonshockable - 1.1191 \times (ROSC > 30) - 0.2629 \times CKD)}$.
Abbreviations as in Table 1.

scenarios are often very challenging, and prognosis is usually unclear in the first few hours after resuscitation. Understanding which unfavorable features are most predictive, and that any combination of 6 or more is a clear "tipping point" toward a very poor prognosis adds value to the previously identified list and algorithm (7). Such knowledge can assist physicians in identifying who are least likely to benefit from aggressive intervention, which can impact the discussion with families regarding realistic expectations. This may also improve resource allocation and direct access to invasive interventions for those more likely to survive.

In total, 3% (73 of 2,508) of patients had a 90% possibility of a ≤10% survival to discharge. If those with 5 unfavorable features are included, a total of 9% (236 of 2,508) have a >70% possibility of a ≤10% rate of survival to discharge. This is a small proportion of the total number of patients, but identifying this subgroup can be valuable regarding appropriate use of invasive procedures such as coronary angiography. These data also suggest that the vast majority of successfully resuscitated cardiac arrest victims, even those with up to 4 unfavorable features, have a reasonable chance to survive to discharge and invasive therapies should be considered.

The vast majority of resuscitated out-of-hospital cardiac arrest STE patients should undergo immediate coronary angiography and PCI. This is currently an American College of Cardiology Foundation/American Heart Association/European Society of Cardiology Class 1 recommendation (16–18). Occasionally, the correct decision might be conservative care without coronary angiography or intervention. However, STE patients make up only 20% to 30% of resuscitated out-of-hospital cardiac arrest adult victims. Approximately three-quarters of those patients successfully resuscitated from out-of-hospital cardiac arrest do not manifest any STE on their post-resuscitation electrocardiogram (2,5,19–21). These are the patients where the value of early coronary angiography and PCI remains controversial and where additional guidance is needed (2,7,22–24). In both groups of patients, those with STE and those without STE on their ECG, the presence of these 3 specific unfavorable features, age >85 years, >30 min to ROSC, and initial nonshockable rhythm, is associated with a survival to discharge rate of <7%. Likewise, if any 6 or more unfavorable features are present on admission, this can be very helpful information to reduce inappropriate resource use and minimize futile care.

For these reasons, we believe this simplified risk assessment tool, which can be calculated at the time of initial presentation or on triaging the patient for transfer to a tertiary care center, adds significant value in providing optimal care for successfully resuscitated but comatose cardiac arrest patients (**Central Illustration**). Discussions concerning expectations and prognosis with other care teams, including interventional cardiology and families, can be centered around individual patient data, which allows more personalized decisions regarding the most appropriate post-resuscitation care.

**STUDY LIMITATIONS.** The retrospective cohort study design and selected patient population represented in the INTCAR database is derived from a group of high-volume, specialized post-resuscitation centers with aggressive post-arrest care interests. The generalizability of such patients could be an issue. The majority of patients had out-of-hospital cardiac arrests, but some were in-hospital arrests and a small number were cardiac arrests in the emergency department. Etiologies of cardiac arrest may vary among these different subpopulations. We were unable to evaluate 3 of the 10 unfavorable features identified in the "Treatment Algorithm for Emergent Invasive Cardiac Procedures in the Resuscitated Comatose Patient" (7). These 3 were not included in the INTCAR database: ongoing CPR, noncardiac causes (e.g., traumatic arrest), and end-stage renal disease. Using CKD as a surrogate for ESRD was not successful, and the direct effect of these 3 factors could not be evaluated in our assessment. The effect on survival to discharge of different institutions approach to the withdrawal of life support measures, especially in patients older than 85 years, is a likely confounder. Finally, the actual number of patients >85 years of age was small (98 of 2,508), and affected the ability to accurately estimate risk of advanced age in some subgroups. We used an expected survival rate of <10% among those initially resuscitated as the cutpoint where further invasive therapies may not be clinically reasonable, but admittedly, a patient's or that patient's family members' cutpoint could be different. Stakeholder opinion and wishes in this regard should be investigated in future studies.

## CONCLUSIONS

The previously published "Treatment Algorithm for Emergent Invasive Cardiac Procedures in the Resuscitated Comatose Patient" (7) was independently refined using an international cardiac arrest registry containing 7 of the 10 unfavorable features suggested in the algorithm. The most unfavorable features were age >85 years, >30 min to ROSC, and an initial nonshockable cardiac arrest rhythm. In

**TABLE 4 Summary of All STE and Non-STE Patient's Characteristics***

| | STE (n = 455) | Non-STE (n = 1,895) | p Value† |
|---|---|---|---|
| Age, yrs | 61.7 ± 12.6 | 62.3 ± 16.2 | 0.26 |
| >85 yrs | 11 (2.4) | 79 (4.2) | 0.10 |
| Male | 362 (79.6) | 1,212 (64.0) | <0.0001 |
| Time-to-ROSC, min | 25.8 ± 17.6 | 24.7 ± 18.9 | 0.88 |
| >30 min | 134 (29.4) | 486 (25.6) | 0.11 |
| Lactate, mmol/l | 7 ± 6.5 | 7.5 ± 6.6 | 0.06 |
| >7 mmol/l | 193 (42.4) | 864 (45.6) | 0.23 |
| pH | 7.2 ± 0.1 | 7.2 ± 0.2 | 0.99 |
| <7.2 | 210 (46.1) | 926 (48.8) | 0.32 |
| Pre-arrest diseases | | | |
| Previously healthy | 127 (27.9) | 273 (14.4) | <0.0001 |
| CAD | 75 (16.5) | 359 (18.9) | 0.25 |
| CHF | 45 (9.9) | 413 (21.8) | <0.0001 |
| Arrythmia | 38 (8.3) | 348 (18.4) | <0.0001 |
| CKD | 35 (7.7) | 296 (15.6) | <0.0001 |
| IDDM | 48 (10.5) | 239 (12.6) | 0.26 |
| Liver disease | 4 (0.9) | 78 (4.1) | <0.001 |
| CVD | 26 (5.7) | 207 (10.9) | <0.001 |
| PVD | 28 (6.1) | 163 (8.6) | 0.10 |
| COPD | 40 (8.8) | 355 (18.7) | <0.0001 |
| Obese | 35 (7.7) | 226 (11.9) | <0.01 |
| NIDDM | 48 (10.5) | 283 (14.9) | 0.02 |
| HTN | 194 (42.6) | 923 (48.7) | <0.0001 |
| Cognitive impairment | 13 (2.9) | 111 (5.9) | <0.01 |
| Solid tumor | 30 (6.6) | 173 (9.1) | 0.09 |
| Malignancy | 32 (7) | 202 (10.7) | 0.02 |
| Neurological disease | 42 (9.2) | 306 (16.1) | <0.001 |
| Pre-CPC | 447 | 1,846 | <0.0001 |
| 1 | 413 (92.3) | 1,493 (80.9) | |
| 2 | 25 (5.6) | 222 (1.0) | |
| 3 | 9 (2.0) | 127 (6.9) | |
| 4 | 0 (0.0) | 4 (0.2) | |
| Witnessed | 394 (86.6) | 1,490 (78.6) | |
| Bystander CPR | 354 (77.8) | 1,417 (74.8) | |
| Initial rhythm | | | <0.0001 |
| VT/VF | 320 (70.3) | 660 (34.8) | |
| PEA/asystole | 116 (25.5) | 1,158 (61.1) | |
| Unknown | 19 (4.2) | 77 (4.1) | |
| Treatment | | | |
| Defibrillation | 358/446 (80.3) | 876/1,864 (47) | <0.0001 |
| TTM used | 410/452 (90.7) | 1,589/1,890 (84.1) | <0.001 |
| CAG | 391/453 (86.3) | 626/1,883 (33.2) | <0.0001 |
| PCI | 295/451 (65.4) | 223/1,888 (11.8) | <0.0001 |
| CABG | 11/452 (2.4) | 33/1,876 (1.8) | 0.34 |
| Revascularization (PCI or CABG) | 303 (66.6) | 251 (13.2) | |
| Outcome | | | |
| Discharge survival | 235/449 (52.3) | 690/1,882 (36.7) | <0.0001 |
| Discharge CPC 1 or 2 of survivors | 200/235 (85.2) | 526/690 (76.2) | <0.0001 |

Values are mean ± SD, n (%), n, or n/N (%). *Excluded patients missing some of the 8 identified risk factors. †Derived 2-sample Student's *t*-test for continuous variables and Fisher exact test for categorical variables. Abbreviations as in **Table 1**.

patients with this triad, survival to hospital discharge is <10%, Likewise, any 6 or more unfavorable features were associated with an equally poor expected outcome.

## AUTHOR DISCLOSURES

Dr. Kern has served as a Science Advisory Board Member for Zoll Medical and Physio-Control, Inc., now part of Stryker, Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**ADDRESS FOR CORRESPONDENCE:** Dr. Karl B. Kern, Division of Cardiology, Sarver Heart Center, University of Arizona, 1501 North Campbell Avenue, P.O. Box 245037, Tucson, Arizona 85724-0001, USA. E-mail: kernk@email.arizona.edu. Twitter: @DrAhmedHarhash.

## PERSPECTIVES

**COMPETENCY IN PATIENT CARE AND PROCEDURAL OUTCOMES:** Among patients successfully resuscitated from out-of-hospital cardiac arrest, the most powerful predictors of adverse outcome are age >85 years, >30 min before return of spontaneous circulation, and an initial nonshockable rhythm.

**TRANSLATIONAL OUTLOOK:** Prospective studies are needed to evaluate the impact of emergent invasive cardiovascular procedures on clinical outcomes in survivors of cardiac arrest.

## REFERENCES

**1.** Virani SS, Alonso A, Benjamin EJ, et al., on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Committee. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. Circulation 2020;141:e139–596.

**2.** Kern KB, Lotun K, Patel N, et al. Outcomes of comatose cardiac arrest survivors with and without ST-segment elevation myocardial infarction: importance of coronary angiography. J Am Coll Cardiol Intv 2015;8:1031–40.

**3.** Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardized treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. Resuscitation 2007;73:29–39.

**4.** Neumar RW, Nolan JP, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication a consensus statement from the International Liaison Committee on Resuscitation (American Heart Association, Australian and New Zealand Council on Resuscitation, European Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Asia, and the Resuscitation Council of Southern Africa); the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Stroke Council. Circulation 2008;118:2452–83.

**5.** Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of- hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Interv 2010;3:200–7.

**6.** Peberdy MA, Donnino MW, Callaway CW, et al., for the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Impact of percutaneous coronary intervention performance reporting on cardiac resuscitation centers: a scientific statement from the American Heart Association. Circulation 2013;128:762–73.

**7.** Rab T, Kern KB, Tamis-Holland JE, et al. Cardiac arrest: a treatment algorithm for emergent invasive cardiac procedures in the resuscitated comatose patient. J Am Coll Cardiol 2015;66:62–73.

**8.** Nielsen N, Wetterslev J, Cronberg T, et al., for the TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med 2013;369:2197–206.

**9.** Seder DB, Patel N, McPherson J, et al. Geriatric experience following cardiac arrest at six interventional cardiology centers in the United States 2006-201: interplay of age, DNR order and outcome. Crit Care Med 2014;42:289–95.

**10.** Karlsson V, Dankiewicz J, Nielsen N, et al. Association of gender to outcome in patients treated with induced hypothermia after out-of-hospital cardiac arrest- a report from the International Cardiac Arrest Registry. Crit Care 2015;19:182–90.

**11.** Bascom KE, Dziodzio J, Vasaiwala S, et al. Derivation and validation of the CADETS score for very early prediction of circulatory etiology death in patients without STEMI after cardiac arrest. Circulation 2018;137:273–82.

**12.** May TL, Lary CW, Riker RR, et al. Variability in functional outcome and treatment practices by center for patients treated with targeted temperature management after out-of-hospital cardiac arrest [published correction in Intensive Care Med 2019;45:1176. Intensive Care Med 2019;45:637–64.

**13.** May T, Skinner K, Unger B, et al. Coronary angiographic findings in women resuscitated from sudden cardiac death. JAHA 2020;9:e015629.

**14.** Reynolds JC, Frisch A, Rittenberger JC, et al. Duration of resuscitation efforts and functional outcome after out-of-hospital cardiac arrest: when should we change do novel therapies? Circulation 2013;128:2488–94.

**15.** 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, Part 10.7: Cardiac Arrest Associated with Trauma. Circulation 2005;112 Suppl OV:IV146–50.

**16.** O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;61:e78–140.

**17.** O'Connor RE, AL Ali AS, Brady WJ, et al. Part 9: acute coronary syndromes: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132 Suppl 2:S483–500.

**18.** Ibanez B, James S, Agewall S, et al. 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the Management of Acute Myocardial Infarction in Patients Presenting With ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2017;39:119–77.

**19.** Dumas FZ, Bougoin W, Geri G, et al. Emergency percutaneous coronary intervention in post-cardiac arrest patients without ST-segment elevation pattern: insights from the PROCAT II Registry. J Am Coll Cardiol Intv 2016;9:1011–8.

**20.** Hollenbeck RD, McPherson JA, Mooney MR, et al. Early cardiac catheterization is associated with improved survival in comatose survivors of cardiac arrest without STEMI. Resuscitation 2014;85:88–95.

**21.** Yannopoulos D, Bartos JA, Aufderheide TP, et al., on behalf of the American Heart Association

Emergency Cardiovascular Care Committee. The evolving role of the cardiac catheterization laboratory in the management of patients with out-of-hospital cardiac arrest. Circulation 2019;139:e530–52.

**22.** Patterson T, Perkins GD, Joseph J, et al. A randomized trial of expedited transfer to a cardiac arrest centre for non-ST elevation ventricular fibrillation out-of-hospital cardiac arrest: the AR-REST pilot randomized trial. Resuscitation 2017;115:185–91.

**23.** Lemkes JS, Janssens GN, van der Hoeven NW, et al. Coronary angiography after cardiac arrest without ST-segment elevation. N Engl J Med 2019;380:1397–407.

**24.** Elfwen L, Lagedal R, Nordberg P, et al. Direct or subacute coronary angiography in out-of hospital cardiac arrest (DISCO)—an initial pilot-study of a randomized clinical trial. Resuscitation 2019;139:253–61.

**KEY WORDS** cardiac arrest, coronary angiography, risk stratification

**APPENDIX** For supplemental figures and a table, please see the online version of this paper.