Predicting the Presence of an Acute Coronary Lesion Among Patients Resuscitated From Cardiac Arrest

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Background—A mechanism to stratify patients resuscitated from a cardiac arrest according to the likelihood of an acute coronary lesion would have significant utility. We thus sought to develop and validate a risk prediction model for the presence of an acute coronary lesion among patients resuscitated from an arrest.

Methods and Results—All subjects undergoing coronary angiography after resuscitation from a cardiac arrest were identified in an ongoing institutional registry from 2009 to 2014. Backwards stepwise selection of candidate covariates was used to create a logistic regression model for the presence of an angiographic culprit lesion and internally validated with bootstrapping. A clinical point score was generated and its diagnostic abilities compared with contemporary measures. Among 247 subjects undergoing coronary angiography after resuscitation from a cardiac arrest, 130 (52%) had an acute lesion in a coronary artery. A multivariable model—including angina, congestive heart failure symptoms, shockable arrest rhythm (ventricular fibrillation/ventricular tachycardia), and ST-elevations—had excellent discrimination (optimism corrected C-Statistic, 0.88) and calibration (Hosmer–Lemeshow P=0.540) for an acute coronary lesion. Compared with electrocardiographic findings alone, a point score based on this model more accurately predicted the presence of an acute lesion among patients resuscitated from a cardiac arrest (integrated discrimination improvement, 0.10; 95% confidence interval, 0.04–0.19; P<0.001).

Conclusions—Patients with a cardiac arrest can be risk stratified for the presence of an acute coronary lesion using 4 easily measured variables. This simple risk score may be used to improve patient selection for emergent coronary angiography among resuscitated patients. (Circ Cardiovasc Interv. 2015;8:e002198. DOI: 10.1161/CIRCINTERVENTIONS.114.002198.)

Key Words: cardiac arrest ■ culprit artery ■ culprit lesion ■ percutaneous coronary intervention

Cardiac arrest is a leading cause of morbidity and mortality in the developed world. Despite advances in emergency medical services, in-hospital mortality among these patients remains unacceptably high. Acute occlusion of an epicardial coronary artery has been strongly associated with cardiac arrest, present in approximately half of patients undergoing angiography in early case series. This has been corroborated with postmortem analyses demonstrating significant coronary artery disease in 39% of patients presenting with a cardiac arrest. Several studies have suggested that the use of coronary angiography with percutaneous coronary intervention may improve hospital survival in patients with a cardiac arrest that have a concomitant acute coronary lesion. Identifying the patients within this group that have a coronary lesion and would thus benefit from emergent coronary angiography, however, has proven challenging.

The current guidelines indicate that emergent coronary angiography and appropriate percutaneous intervention be performed in patients with a cardiac arrest that have persistent electrocardiographic evidence of ischemia, manifested as ST-elevations. These same guidelines suggest that others resuscitated from a cardiac arrest without definite electrocardiographic evidence of ischemia may be considered for emergent angiography. Previous research has demonstrated that a standard ECG has a poor negative predictive value for the presence of an acute coronary lesion in those resuscitated from a cardiac arrest. Further, symptom reporting in this setting is not uniform and often dependent on the presence of bystanders witnessing the event. The decision to proceed with emergent coronary angiography is thus often made with incomplete information. Because of this, an improved mechanism to stratify patients according to the likelihood of a concomitant coronary lesion would have significant clinical utility in this population.

The present study sought to identify clinical characteristics associated with an acute coronary artery culprit lesion among patients resuscitated from a cardiac arrest in a real-world...
WHAT IS KNOWN

- Current guidelines indicate that emergent coronary angiography be performed in patients with a cardiac arrest that have persistent electrocardiographic evidence of ischemia, manifested as ST-elevations.
- Current guidelines suggest that others resuscitated from a cardiac arrest without definite electrocardiographic evidence of ischemia may be considered for emergent angiography.
- Because of this, an improved mechanism to stratify patients according to the likelihood of a concomitant coronary lesion would have significant clinical utility in this population.

WHAT THE STUDY ADDS

- Four easily captured variables are able to effectively stratify patients according to their likelihood of having an angiographic culprit lesion after resuscitation from a cardiac arrest.
- Compared with factors used in contemporary clinical practice, a simple risk score based on these characteristics should significantly improve patient selection for emergent coronary angiography among those treated for this condition.

Methods

Population
All patients presenting to an academic medical center (Massachusetts General Hospital) that undergo coronary angiography are included in an ongoing institutionally sponsored registry that was initiated in 2004 and included data regarding an antecedent cardiac arrest in 2009. This registry includes data fields for the National Cardiovascular Data Registry (NCDR) CathPCI registry. The present project focused on consecutive patients within this cohort that suffered an out-of-hospital or in-hospital cardiac arrest and were subsequently selected for coronary angiography within 24 hours of resuscitation by their treating clinicians. To determine the proportion of patients that were selected for angiography, International Classification of Disease codes (ICD-9: 427.5) for cardiac arrest were used to identify the total number of patients treated for this condition during the same time period within a hospital administrative data set. Those that were successfully resuscitated from an arrest and identified within this data set were considered potential candidates for coronary angiography. The present project has been reviewed and approved with a waiver of consent from the institutional review board at Partners Healthcare. Furthermore, the present study complies with the Declaration of Helsinki.

Measurements
Clinical and procedural information was abstracted from the electronic medical record and included in the registry. Definitions for symptoms and comorbid conditions were derived from the NCDR CathPCI data definitions (https://www.ncdr.com, accessed May 1, 2014). For example, heart failure was defined as “physician documentation or report of any of the following clinical symptoms of heart failure: unusual dyspnea on light exertion; recurrent dyspnea occurring in the supine position; fluid retention; the description of rales, jugular venous distension, pulmonary edema on physical examination; or pulmonary edema on chest x-ray” based on these standardized definitions. Documentation of symptoms was ascertained from electronic notes authored by the treating clinicians, who used all information available at the time of presentation. A symptom was presumed to be absent by the treating clinicians if it could not be corroborated by the subject or a bystander. Similarly, the initial arrest rhythm was ascertained from the same electronic notes that included interpretation of telemetry data obtained from emergency medical services or the inpatient setting. Electrocardiograms obtained on hospital presentation for outpatients or immediately after return of spontaneous circulation for inpatients were independently evaluated by a cardiologist blinded to the coronary angiogram. ST-deviations (≥0.1 mV) in 2 contiguous anatomic leads were considered significant, consistent with current professional society guidelines. Similarly, a left bundle branch block was coded using previously published criteria. The decision to proceed with coronary angiography was determined by the treating clinicians irrespective of neurological status and did not follow a formal algorithm. After the procedure was performed, a blinded interventional cardiologist reviewed the coronary angiograms to ascertain the presence or absence of a culprit lesion within an epicardial coronary artery. For the purposes of this evaluation, an acute culprit lesion was defined as a stenosis (≥70%) of a major coronary artery (≥2 mm) with reduced blood flow to the distal vessel (TIMI grade flow <3). Complete occlusion of an epicardial vessel with bridging or contralateral collateral circulation suggestive of a chronic total occlusion was not considered an acute culprit lesion. Any definition for an acute culprit lesion is likely to be somewhat subjective, and the proposed definition in this study attempts to reduce the subjectivity as much as possible. In addition, this definition was based on previously published work. Among patients without an acute coronary lesion, the electronic medical record was reviewed to determine an alternative pathogenesis for the cardiac arrest as defined by the treating clinicians. All study data were collected and managed using the Research Electronic Data Capture (REDCap) reporting system hosted at Partners Healthcare.

Analysis
The study population was stratified based on the presence or absence of an acute culprit lesion. Summary statistics were reported as means with standard deviations (SD) for continuous variables or medians and interquartile ranges for non-normally distributed continuous data. T-tests and Kruskal–Wallis ANOVA by ranks were used to compare normally and non-normally distributed continuous variables, respectively. Chi-squared tests were used to evaluate differences in proportions. Variables that were found to be statistically significant (P<0.05) between the groups in a univariate analysis were considered as candidate covariates for a risk prediction model. A final logistic regression model was created from these candidate covariates by refitting the model, including backward selection in 1000 bootstrap samples with replacement, using a conservative P value (P<0.05) for retention. A sensitivity analysis was performed using forward stepwise selection to create the logistic model using the same P value (P<0.05) for inclusion. Forward and backward stepwise selection resulted in the creation of a model with identical covariates. Discrimination of the resulting model was characterized using a receiver operator curve. Calibration of the model was assessed after fitting a polynomial regression line between the predicted and observed risk of an acute coronary artery lesion. Goodness of fit testing was also performed using the Hosmer–Lemeshow test. The initial model was fitted to the entire data set, and validation was performed by refitting the model in 1000 bootstrap samples with replacement. This method of model validation has been found to have lower variability and bias potential compared with traditional split-sample or k-fold validation. The final reported estimates of model discrimination and calibration were reduced to account for optimism. Model coefficients were adjusted based on the calculation of the linear calibration slope to adjust for overfitting based on previously described methods. To support routine clinical use, we then
developed a risk score based on a points system with weights derived from the coefficients in the final clinical model. The point score was subsequently compared with electrocardiographic evidence of ischemia alone to compare discriminatory ability (C-statistic), as well as the integrated discrimination improvement of the prediction model. A sensitivity analysis was performed assessing the subjective (chest pain/heart failure) and objective (shockable rhythm/ST-elevation) components of the model. Additional sensitivity analyses were performed only in subjects without ST-elevations. All statistical analyses were performed using STATA 12.1 (Stata Corp, College Station, TX) or R 3.0.3 (http://www.R-project.org). A P value <0.05 was considered statistically significant. All authors take full responsibility for the integrity of the data and agree to the article as written.

Results

Population
Between May 2009 and February 2014, 1815 subjects suffered a cardiac arrest, with 787 (43%) of these arrests occurring in the outpatient setting. A review of the records indicated that 397 (50%) survived an out-of-hospital arrest and 727 (71%) survived in an in-hospital arrest for a total of 1124 patients. Of the resuscitated patients, 149 (38%) out-of-hospital arrest and 98 (13%) in-hospital arrest patients, together totaling 247 (22%) subjects, underwent coronary angiography within 24 hours and served as the study population for the remainder of the analysis (Figure 1). The overwhelming majority of patients not selected for coronary angiography were deemed to have a noncardiac pathogenesis for their arrest (64%). Among those selected for coronary angiography, 130 (53%) had an acute culprit lesion in a major epicardial coronary artery. The documented etiologies for a cardiac arrest among the 117 (47%) patients without an angiographic culprit lesion are listed in the Table in the Data Supplement.

Demographics
The demographic data for the analyzed patient population is presented in Table 1. Focusing on the subjects selected for coronary angiography, subjects with an acute culprit lesion were more likely to present with an arrest rhythm responsive to defibrillation, such as ventricular fibrillation or ventricular tachycardia, than those without an acute culprit lesion (P<0.001). Similarly, a higher proportion of patients with an acute culprit lesion presented with angina (P<0.001) and symptoms consistent with congestive heart failure (P=0.001) before or after resuscitation from the arrest. The median level of cardiac biomarkers obtained on presentation was also statistically greater among those with an acute culprit lesion, though the numeric difference between the groups was small (P=0.042). However, the peak median level of troponin was clinically and statistically greater among patients with an acute culprit lesion (P<0.001). Initiation of therapeutic hypothermia was similar between the 2 groups, though percutaneous revascularization was significantly more common among patients with an acute culprit lesion (P<0.001). Finally, in-hospital mortality was numerically and statistically similar between those with and without an acute culprit lesion (P=0.55).

ECG
The electrocardiographic data for the analyzed patient population is presented in Table 2. Focusing on the subjects selected for coronary angiography, electronically archived electrocardiograms obtained immediately after presentation or the return of spontaneous circulation were available for 195 (79%) of the subjects. The demographic characteristics between those with and without an electronically archived ECG were similar (data not shown). Among patients with an ECG available for review, the median QRS duration was longer in patients without an acute culprit lesion (P=0.029). The presence of ST-elevation in 2 contiguous leads, however, was significantly greater among those with an acute culprit lesion (P<0.001).

Angiography
The angiographic findings for the cohort selected for coronary angiography are reproduced in Table 3. Subjects with an acute culprit lesion had a higher rate of significant (>70%) stenosis in the left anterior descending artery (P<0.001) and right coronary artery (P<0.001). Among patients with an acute coronary lesion, obstruction of flow in the left anterior descending artery was the most common (44%) followed by acutely reduced flow in the right coronary artery (30%).

Model Development
A logistic regression model was created using covariates from the clinical and electrocardiographic data that reached

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**Figure 1.** Consort diagram. The diagram indicates the total number of cardiac arrest subjects identified stratified by an in-hospital or out-hospital event. Subjects were then divided into those that were successful resuscitated and taken for angiography, identified by the red boxes. The patients within the brackets are the main subpopulation under investigation for the present analysis.
# Table 1. Demographic Characteristics

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>All Arrests</th>
<th>Arrests Undergoing Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angio (n=247)</td>
<td>No Angio (n=877)</td>
</tr>
<tr>
<td>Age, y</td>
<td>62±13</td>
<td>62±19</td>
</tr>
<tr>
<td>Male</td>
<td>531 (61)</td>
<td>179 (72)</td>
</tr>
<tr>
<td>Race</td>
<td>&lt;0.001</td>
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<tr>
<td>Asian</td>
<td>2 (2)</td>
<td>25 (3)</td>
</tr>
<tr>
<td>Black</td>
<td>12 (6)</td>
<td>16 (2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10 (4)</td>
<td>42 (5)</td>
</tr>
<tr>
<td>White</td>
<td>188 (81)</td>
<td>790 (90)</td>
</tr>
<tr>
<td>Other</td>
<td>21 (9)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Arrest location</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>In-hospital</td>
<td>98 (40)</td>
<td>629 (72)</td>
</tr>
<tr>
<td>Out-of-hospital</td>
<td>149 (60)</td>
<td>248 (28)</td>
</tr>
<tr>
<td>Arrest rhythm</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>115 (47)</td>
<td>120 (14)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>41 (17)</td>
<td>87 (10)</td>
</tr>
<tr>
<td>Pulseless electric activity</td>
<td>44 (18)</td>
<td>308 (35)</td>
</tr>
<tr>
<td>Asystole</td>
<td>13 (5)</td>
<td>300 (34)</td>
</tr>
<tr>
<td>Unknown</td>
<td>34 (14)</td>
<td>62 (7)</td>
</tr>
<tr>
<td>Presenting complaint</td>
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</tr>
<tr>
<td>Angina</td>
<td>127 (51)</td>
<td>...</td>
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<tr>
<td>Complicating symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>109 (44)</td>
<td>...</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>168 (68)</td>
<td>...</td>
</tr>
<tr>
<td>Medical comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>30 (13)</td>
<td>86 (10)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>31 (13)</td>
<td>135 (15)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>64 (26)</td>
<td>230 (26)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>199 (81)</td>
<td>326 (37)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>167 (67)</td>
<td>490 (56)</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>43 (17)</td>
<td>79 (9)</td>
</tr>
<tr>
<td>Prior congestive heart failure</td>
<td>40 (16)</td>
<td>159 (18)</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>71 (29)</td>
<td>105 (12)</td>
</tr>
<tr>
<td>Prior percutaneous intervention</td>
<td>44 (18)</td>
<td>74 (8)</td>
</tr>
<tr>
<td>Prior coronary artery bypass grafting</td>
<td>24 (10)</td>
<td>77 (9)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>23 (9)</td>
<td>112 (13)</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>38 (15)</td>
<td>99 (11)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco</td>
<td>62 (25)</td>
<td>383 (44)</td>
</tr>
<tr>
<td>Ethanol</td>
<td>37 (15)</td>
<td>...</td>
</tr>
<tr>
<td>Illicit drugs</td>
<td>33 (13)</td>
<td>...</td>
</tr>
<tr>
<td>Laboratory values</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>13 (11–15)</td>
<td>...</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.2 (0.9–1.5)</td>
<td>...</td>
</tr>
<tr>
<td>Creatine kinase–myocardial band, ng/mL</td>
<td>12 (4–47)</td>
<td>...</td>
</tr>
<tr>
<td>Troponin T (initial), ng/mL</td>
<td>0.2 (0–1.2)</td>
<td>...</td>
</tr>
<tr>
<td>Troponin T (peak), ng/mL</td>
<td>2.1 (0.4–7.3)</td>
<td>...</td>
</tr>
<tr>
<td>Inpatient management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic hypothermia</td>
<td>54 (22)</td>
<td>140 (16)</td>
</tr>
<tr>
<td>Percutaneous revascularization</td>
<td>139 (56)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Inpatient mortality</td>
<td>82 (33)</td>
<td>348 (40)</td>
</tr>
</tbody>
</table>

All data presented as mean±standard deviation or median (intraquartile range) for continuous variables and number (percentage) for categorical variables. Missing data among those not sent for coronary angiography is represented by ellipses (...).
statistical significance in a univariate analysis among those selected for coronary angiography. To simplify the candidate covariates for routine clinical use, the initial arrest rhythm was incorporated into the model selection process as the presence or absence of a rhythm responsive to defibrillation, such as ventricular fibrillation or ventricular tachycardia. After backwards selection, angina (odds ratio, 3.49; 95% confidence interval [CI], 1.03–11.84), congestive heart failure symptoms (odds ratio, 3.58; 95% CI, 0.86–14.88), shockable arrest rhythm (odds ratio, 5.26; 95% CI, 1.26–21.89), and ST-elevation in 2 contiguous leads after return of spontaneous circulation (odds ratio, 9.65; 95% CI, 2.54–36.74) were retained in the model. The original and bias corrected beta coefficients for these covariates are listed in Table 4.

Model Assessment
The C-statistic for the model in the entire population analyzed was calculated as 0.90 and 0.88 after correcting for optimism. A fitted polynomial regression line between the predicted risk and observed risk of an epicardial coronary artery lesion suggested appropriate calibration of the bias-corrected model (Figure 2, Hosmer–Lemeshow P=0.540).

Clinical Utility
The most commonly used variable to assess the likelihood of an acute coronary lesion in contemporary clinical practice is electrocardiographic evidence of ischemia manifested as ST-elevations in 2 contiguous leads. Because of this, the clinical utility of the derived point score was compared with a model that included ST-elevation alone. The clinical point score was found to have increased discriminatory ability (C-statistic, 0.88; 95% CI, 0.83–0.92) compared with the presence of ST-elevations (C-statistic, 0.80; 95% CI, 0.74–0.85; P<0.001).

Table 2. Electrocardiographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Arrests</th>
<th></th>
<th>Arrests Undergoing Angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angio (n=247)</td>
<td>No Angio (n=877)</td>
<td>P Value</td>
</tr>
<tr>
<td>Rate</td>
<td>86 (68–102)</td>
<td>86 (69–104)</td>
<td>0.529</td>
</tr>
<tr>
<td>Rhythm</td>
<td></td>
<td>0.229</td>
<td></td>
</tr>
<tr>
<td>Sinus</td>
<td>147 (75)</td>
<td>617 (80)</td>
<td>0.088</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>40 (21)</td>
<td>112 (15)</td>
<td>0.006</td>
</tr>
<tr>
<td>Junctional rhythm</td>
<td>6 (3)</td>
<td>18 (2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventricular rhythm</td>
<td>2 (1)</td>
<td>20 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intervals, ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>166 (150–186)</td>
<td>160 (138–155)</td>
<td>0.006</td>
</tr>
<tr>
<td>QRS</td>
<td>104 (92–129)</td>
<td>98 (86–120)</td>
<td>0.083</td>
</tr>
<tr>
<td>QTc</td>
<td>466 (430–493)</td>
<td>460 (429–499)</td>
<td>0.001</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td></td>
<td>0.241</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>154 (79)</td>
<td>699 (83)</td>
<td>0.001</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>13 (7)</td>
<td>48 (6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Right bundle branch block</td>
<td>28 (14)</td>
<td>87 (10)</td>
<td>0.001</td>
</tr>
<tr>
<td>ST-depression (2 contiguous leads)</td>
<td>52 (27)</td>
<td>58 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST-elevation (2 contiguous leads)</td>
<td>84 (43)</td>
<td>28 (3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ST deviation is defined as >1 mm in 2 contiguous electrocardiographic leads. All data presented as median (intraquartile range) for continuous variables and number (percentage) for categorical variables.

Table 3. Angiographic Characteristics

<table>
<thead>
<tr>
<th>Culprit</th>
<th>No Culprit</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Significant stenosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main (&gt;50%)</td>
<td>16 (13)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Left anterior descending (&gt;70%)</td>
<td>77 (63)</td>
<td>24 (24)</td>
</tr>
<tr>
<td>Left circumflex (&gt;70%)</td>
<td>44 (36)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>Right coronary artery (&gt;70%)</td>
<td>72 (59)</td>
<td>37 (37)</td>
</tr>
<tr>
<td>Culprit location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main</td>
<td>7 (5)</td>
<td>...</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>57 (44)</td>
<td>...</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>20 (15)</td>
<td>...</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>39 (30)</td>
<td>...</td>
</tr>
<tr>
<td>Diagonal branch</td>
<td>3 (2)</td>
<td>...</td>
</tr>
<tr>
<td>Obuse marginal</td>
<td>4 (3)</td>
<td>...</td>
</tr>
</tbody>
</table>

All data presented number (percentage).
Similarly, the incremental predictive capability of the point score for an acute culprit lesion was high as assessed by integrated discrimination improvement (0.10; 95% CI, 0.02–0.17) with a relative integrated discrimination improvement of 0.28 (95% CI, 0.09–0.72). A sensitivity analysis suggests that the discriminatory ability of the subjective components of the model (C-statistic, 0.69; 95% CI, 0.62–0.75) were lower than a model only including the objective components (C-statistic, 0.86; 95% CI, 0.81–0.91; P<0.001). The integrated discriminatory improvement of the complete 4-component model, however, is numerically greater than the objective 2-component model alone (0.04; 95% CI, −0.01 to 0.09), suggesting that the complete model has the highest clinical utility. An additional sensitivity analysis limited to patients without ST-elevations demonstrated that the 4-component model had moderate discriminatory ability (C-statistic, 0.74; 95% CI, 0.68–0.81). Further, the incremental predictive capability of the point score in this limited population was high when compared with the standard ECG alone, as assessed by the integrated discrimination improvement (0.19; 95% CI, 0.09–0.35).

**Discussion**

We evaluated the clinical characteristics of consecutive patients resuscitated from a cardiac arrest that subsequently underwent emergent coronary angiography at a large academic medical center. As the data demonstrate, a multivariable model, including 4 simple clinical parameters, has excellent discrimination and calibration for an acute culprit lesion in this population. Compared with measures used in contemporary clinical practice and recommended by professional society guidelines, a point score derived from this model has improved predictive capabilities and the potential to significantly enhance patient selection for emergent coronary angiography among those resuscitated from a cardiac arrest.

Cardiac arrest represents a clinical manifestation of a wide variety of pathophysiological processes. Previous research has suggested that acute occlusion of an epicardial coronary artery was present in 73% of subjects with a cardiac arrest.23,24 More recent studies, however, have suggested that only 39% of unselected subjects dying of a cardiac arrest had a likely ischemic pathogenesis at postmortem examination.3 The present study of consecutive patients undergoing angiography after resuscitation from a cardiac arrest found a slightly higher predominance of coronary lesions, perhaps reflecting that these individuals were selected for angiography based on the clinical suspicion of the treating physicians. Prompt intervention to address the underlying cause of a cardiac arrest is critical to improve survival, particularly for those with an acute occlusion of an epicardial coronary artery. Several studies have shown that prompt percutaneous intervention improves in-hospital survival among patients resuscitated from a cardiac arrest precipitated by an acute culprit lesion.4,6,7 European consensus statements have thus suggested that most patients resuscitated from a cardiac arrest should undergo urgent (<2 hours) coronary angiography.25 Professional guidelines in the United States have not yet embraced these recommendations.8,10 Because of this, a mechanism to risk stratify patients according to the likelihood of an acute culprit lesion could have significant clinical utility.

Contemporary professional society guidelines indicate that emergent coronary angiography may be performed in all resuscitated subjects with persistent electrocardiographic evidence of ischemia.8 Those without ongoing electrocardiographic evidence of ischemia after resuscitation, however, can be considered for emergent angiography at the discretion of the treating physician. Previous research has demonstrated that electrocardiographic evidence of ischemia, primarily

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original Coefficient</th>
<th>Original OR (95% CI)</th>
<th>Bias-Corrected Coefficient</th>
<th>Bias-Corrected OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-3.881</td>
<td>-3.393</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>1.429</td>
<td>4.17 (1.23–14.17)</td>
<td>1.249</td>
<td>3.49 (1.03–11.84)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.459</td>
<td>4.30 (1.04–17.87)</td>
<td>1.276</td>
<td>3.58 (0.86–14.88)</td>
</tr>
<tr>
<td>Shockable arrest rhythm</td>
<td>1.899</td>
<td>6.68 (1.61–27.79)</td>
<td>1.660</td>
<td>5.26 (1.26–21.89)</td>
</tr>
<tr>
<td>ST-elevation</td>
<td>2.593</td>
<td>13.37 (3.51–50.89)</td>
<td>2.267</td>
<td>9.65 (2.54–36.74)</td>
</tr>
</tbody>
</table>

Bias-corrected coefficients were determined via multiplication by the calibration slope (0.8743). CI indicates confidence interval; and OR, odds ratio.
manifested as ST-elevations, has a poor negative predictive value for an epicardial coronary lesion.\textsuperscript{6,11–13} Despite this, ST-elevations are one of the most important determinants of whether a resuscitated patient undergoes emergent angiography in contemporary clinical practice.\textsuperscript{26} In the present study, ST-elevations have a moderate discriminatory ability for an acute culprit lesion. The addition of other clinical parameters significantly improves the ability to select appropriate patients for emergent angiography.

Several clinical characteristics are associated with an increased probability of an acute culprit lesion among subjects resuscitated from a cardiac arrest. Interestingly, initial cardiac biomarker levels do not discriminate among patients with and without an acute culprit lesion and peak values return several hours after hospital presentation, eliminating the potential for emergent coronary angiography. After multivariable adjustment, 4 clinical parameters with significant prognostic potential were identified in the present study: angina, acute congestive heart failure symptoms, shockable rhythm, and ST-elevations—conveniently abbreviated ACS.\textsuperscript{3} Symptoms of angina and heart failure before or after resuscitation from a cardiac arrest represent a logical clinical manifestation of an acute culprit lesion. Because of this, these symptoms have been incorporated into international guidelines as reasons to consider emergent angiography among resuscitated patients even in the absence of electrocardiographic changes.\textsuperscript{27} An arrest precipitated by ventricular fibrillation or ventricular tachycardia is also associated with an increased likelihood of a concomitant coronary lesion, again consistent with observational findings in prior studies.\textsuperscript{28} Fortunately, each of these clinical parameters incorporated into the risk prediction model are easy to obtain in an emergent clinical setting. Simplification of the model to determine whether the initial arrest rhythm required defibrillation could even be deduced by untrained bystanders with an automatic external defibrillator. Despite the simplicity of the model, it still provides incremental prognostic information over diagnostic tests used in contemporary clinical practice.

We think that the presented clinical prediction score represents a significant improvement in risk stratification among patients resuscitated from a cardiac arrest. Compared with ST-elevations alone, the presented risk score has much greater discriminatory ability based on the integrated discriminatory improvement. Subjects with risk scores of ≤1 have an exceptionally low risk of having an acute culprit lesion and perhaps may be excluded from emergent coronary angiography after appropriate clinical evaluation. Interventions focusing on identifying other reversible causes of an arrest may be more useful for such patients. Those with higher scores (>1), however, may benefit from invasive angiography even in the absence of electrocardiographic changes. Prospective studies evaluating this approach would serve to further validate the clinical risk model.

Table 5. Point Score (ACS\textsuperscript{2})

<table>
<thead>
<tr>
<th>Variable</th>
<th>Point Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure symptoms</td>
<td>1</td>
</tr>
<tr>
<td>Shockable rhythm (ventricular fibrillation/ventricular tachycardia)</td>
<td>1</td>
</tr>
<tr>
<td>ST-elevation (2 contiguous leads)</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure 3. Rates of coronary lesion stratified by point score. Observed proportion of all subjects with an epicardial coronary lesion stratified by the derived cumulative point score abbreviated ACS\textsuperscript{2} (A). The numbers above each bar indicate the number of subjects with an angiographic culprit lesion over the total number of patients with a given point score. The same findings for those with ST-elevations (B); the score for those without ST-elevations (C).
Limitations

The present study should be interpreted within the context of several limitations. As with previous research on this topic, the cohort included in the present analysis was selected from consecutive patients with a cardiac arrest that survived to hospitalization and were subsequently selected for emergent coronary angiography. Subjects with a significant burden of coronary thrombus, for example, may have a higher incidence of out-of-hospital mortality and would not be included in the present study. Similarly, patients with an explicit noncardiac pathogenesis for an arrest would not be selected for angiography by the treating clinicians and thus excluded from our analysis. The neurological status immediately after resuscitation was not available for all subjects within this cohort, though relatively low rates of therapeutic hypothermia suggest a small proportion of patients had significant impairment after resuscitation. Post-resuscitation electrocardiograms were not available for a modest proportion of patients in our cohort raising the possibility of selection bias in the analyzed sample. However, patients without electronic electrocardiograms were similar in all measured variables to those with electrocardiograms. Further, there are inherent limitations in identifying an angiographic culprit lesion. The present study used a specific definition that was used consistently across all subjects, but a broader definition may impact the ultimate results. Subjects were drawn from an urban tertiary care medical center, and validated internally, and thus may not be generalizable to other institutions where alternative etiologies for cardiac arrest may predominate. External validation would strengthen the results of the article, but the internal validation with correction for optimization that was performed has been previously shown to be robust. Finally, the modest sample size limits our power to detect other clinical characteristics that may be associated with a culprit lesion and thus be included in our model. It is important to note, however, that this is the largest reported cohort used to develop a risk score for an acute coronary lesion after resuscitation from a cardiac arrest. Further studies incorporating larger patient populations should be designed to address these limitations and externally validate the presented findings.

Conclusions

Four easily captured variables are able to effectively stratify patients according to their likelihood of having an angiographic culprit lesion after resuscitation from a cardiac arrest. When compared with factors used in contemporary clinical practice, this simple risk score should significantly improve patient selection for emergent coronary angiography among those treated for this condition.

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Disclosures

None.

References


Predicting the Presence of an Acute Coronary Lesion Among Patients Resuscitated From Cardiac Arrest

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Data Supplement (unedited) at:
http://circinterventions.ahajournals.org/content/suppl/2015/10/13/CIRCINTERVENTIONS.114.002198.DC1
### Supplemental Table

Cardiac arrest etiologies among patients without a culprit lesion

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrhythmia</td>
<td>62 (53)</td>
</tr>
<tr>
<td>Primary Cardiac Arrhythmia</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Scar-Mediated Ventricular Tachycardia</td>
<td>58 (49)</td>
</tr>
<tr>
<td>Cardiomyopathy (Non-Ischemic)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Coronary Vasospasm</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Drug Overdose</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Pulmonary Disease</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Valvular Heart Disease</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (9)</td>
</tr>
</tbody>
</table>

- All data presented as number (percentage) for categorical variable