Clinical paper

Prognostic implications and outcomes of cardiac arrest among contemporary patients with STEMI treated with PCI

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Abstract

Background: Cardiac arrest (CA) complicating ST-elevation myocardial infarction (STEMI) is associated with a disproportionately higher risk of mortality. We described the contemporary presentation, management, and outcomes of CA patients in the era of primary percutaneous coronary intervention (PCI).

Methods: We reviewed 1,272 consecutive STEMI patients who underwent PCI between 1/1/2011-12/31/2016 and compared characteristics and outcomes between non-CA (N = 1,124) and CA patients (N = 148), defined per NCDR definitions as pulseless arrest requiring cardiopulmonary resuscitation and/or defibrillation within 24-hr of PCI.

Results: Male gender, cerebrovascular disease, chronic kidney disease, in-hospital STEMI, left main or left anterior descending culprit vessel, and initial TIMI 0 or 1 flow were independent predictors for CA. CA patients had longer door-to-balloon-time (106 [83, 139] vs. 97 [74, 121] minutes, p = 0.003) and greater incidence of cardiogenic shock (48.0% vs. 5.9%, p < 0.001), major bleeding (25.0% vs. 9.4%, p < 0.001), and 30-day mortality (16.2% vs. 4.1%, p < 0.001). Risk score for 30-day mortality based on presenting characteristics provided excellent prognostic accuracy (area under the curve = 0.902). However, over long-term follow-up of 4.5 ± 2.4 years among hospital survivors, CA did not portend any additional mortality risk (HR: 1.01, 95% CI: 0.56 – 1.82, p = 0.97).

Conclusions: In a contemporary cohort of STEMI patients undergoing primary PCI, CA occurs in >10% of patients and is an important mechanism of mortality in patients with in-hospital STEMI. While CA is associated with adverse outcomes, it carries no additional risk of long-term mortality among survivors highlighting the need for strategies to improve the in-hospital care of STEMI patients with CA.

Keywords: Cardiac arrest, ST-elevation myocardial infarction, Outcomes

Introduction

ST-elevation myocardial infarction (STEMI) complicated by cardiac arrest (CA) is associated with significant morbidity and mortality in the United States. Despite system of care advances resulting in great improvement in outcomes among patients with uncomplicated STEMI, rates of CA are rising. The efficacy and feasibility of primary percutaneous coronary intervention (PCI) among patients with STEMI and CA have been well-established and current guidelines...
recommend use of emergent angiography and PCI among appropriate patients. However, in spite of this and recent advances in the care of these patients including early initiation of targeted temperature management, mortality remains significantly elevated in comparison to patients with STEMI without CA. 

Although registries and state reporting systems attempt to adjust for variables predicting mortality, it remains difficult to adjust for conditions that portend a very high risk of mortality such as CA and cardiogenic shock associated with STEMI presentation. Importantly, there is suggestion that among states where public reporting is mandated, mortality among patients with STEMI complicated by CA or cardiogenic shock is lower among those who undergo PCI but higher among those who do not. This “risk avoidance creep,” in which sicker patients are precluded from potentially life-saving interventions due to concern for negative outcomes, is balanced by the important implications of resource allocation and utilization when providing care that may be futile.

As such, this highlights the importance of accurately describing this high risk patient population, as this would delineate current practice patterns, understand deficiencies, and may improve health care delivery and outcomes. Although several published reports have described presenting characteristics and outcomes of this population via large database analyses or international registries, minimal data within a contemporary regional system of care in the era of primary PCI exist. Accordingly, we assessed presentation characteristics, management, and predictors of short- and long-term outcomes in patients presenting with STEMI who undergo PCI and compared them between those with and without CA.

**Methods**

**Patient cohort, definitions, and outcomes**

We performed an observational, single-center, registry-based study of consecutive patients with STEMI treated with primary PCI from 1/1/2011-12/31/2016. No patients were excluded. We identified patients within our registry who had CA defined by the American College of Cardiology National Cardiovascular Data Registry (ACC NCDR) definition as pulseless clinical scenarios that were pulseless electrical activity, bradycardic, or tachycardic arrests requiring cardiopulmonary resuscitation and/or emergency defibrillation within 24-hr prior to PCI. Baseline and presentation characteristics, procedural data, in-hospital management, and short- and long-term outcomes were collected prospectively and adjudicated by the standards of the ACC NCDR CathPCI Registry. We compared these characteristics and outcomes of patients with and without CA. Survival status was ascertained by review of the medical record and follow-up phone calls and/or Google obituary searches for patients in whom survival status was not available in the medical record. Mean follow-up was 4.5 ± 2.4 years with survival status complete in 98.9% (N = 1258) at 30-days, 95.2% (N = 1211) at 1-year, and 83.8% (N = 1066) of the population at 3-years.

**Statistical analysis**

Percentages and means ± standard deviation or median with interquartile range were computed for categorical and continuous variables, respectively. Categorical variables were compared using the Chi-square test or Fisher’s exact tests while continuous variables were analyzed using the two-tailed Student’s t test or the Mann–Whitney-U test, when appropriate.

Logistic regression was performed to assess for predictors of CA. All variables were initially assessed in univariable logistic regression analysis; variables with a p-value < 0.10 and variables deemed clinically important were included in multivariable logistic regression analysis with final model determined using stepwise regression. Collinearity was assessed with variance inflation factors. We then performed logistic regression to assess for predictors of 30-day mortality among CA patients. Variables were similarly selected using univariable logistic regression analysis. Due to a large number of important predictors, various model selection strategies were employed to prevent overfitting the final model, including stepwise regression, best subset selection, ridge regression, LASSO, and bootstrapping. However, predictive accuracy was limited due to the sample size. We instead used these variables to design a receiver operator characteristic (ROC) curve that predicted probability of 30-day mortality among CA patients based on a score comprised of the sum of the weighted odds ratios for each variable. To determine cut-points for continuous variables to make the risk score, sensitivity and specificity values were calculated for all possible cut-off points and plotted as a ROC. The point on the ROC curve with the greatest Youden’s index was selected as the cut-point. We then applied the NCDR CathPCI Risk Score System to our population and assessed its predictive accuracy in comparison.

We used Kaplan–Meier life tables and the log-rank test to compare mortality between patients with and without CA and among those that survived to hospital discharge. To determine important predictors for long-term mortality among hospital survivors, multivariable Cox proportional hazard models were constructed with variable selection similar to above using stepwise regression and then forcing cardiac arrest into the final model.

Analyses were performed using R version 3.6.3 Software (R Foundation for Statistical Computing, Vienna, Austria). This study was approved by the Institutional Review Board and waiver of written informed consent was provided.

**Results**

**Baseline characteristics, presentation characteristics, and angiographic findings**

From January 1, 2011, to December 31, 2016, there were 1,272 patients with STEMI who underwent primary PCI of which 1,193 were diagnosed in an Emergency Room and 79 (6.2%) while already hospitalized. In total, 148 patients (11.6%) had CA (Table 1). Patients with STEMI and CA were more likely to have a history of heart failure, valve surgery, cerebrovascular disease, peripheral artery disease, and chronic kidney disease with glomerular filtration rate <60 mL/min/1.73 m² and less likely to have a family history of coronary artery disease.

Among the 148 CA patients, 104 patients (70.3%) had out-of-hospital CA, 24 (16.2%) in the cardiac catheterization laboratory, and 20 (13.5%) while hospitalized for another reason. The presenting rhythm was unstable ventricular tachycardia or fibrillation in 132 (89.2%) patients with 52 (35.1%) patients requiring cardiopulmonary resuscitation for greater than 5 min. There was a high rate of poor cerebral performance category [1: 62 (41.9%), 2: 29 (19.6%), 3: 22 (14.9%), 4: 35 (23.6%)] and most patients had a reduced pH (7.28
### Table 1 – Baseline characteristics, presentation, and angiographic findings of STEMI patients with and without cardiac arrest.

|                               | No cardiac arrest  | Cardiac arrest                  | p-Value |
|-------------------------------|--------------------|---------------------------------|---------|
|                               | (N = 1124)         | (N = 148)                       |         |
| **Baseline characteristics**  |                    |                                 |         |
| Age (years)                   | 61 [53, 70]        | 62 [52, 69]                     | 0.833   |
| Male (%)                      | 758 (67.4)         | 110 (74.3)                      | 0.110   |
| Body mass index               | 29.6 ± 6.2         | 28.8 ± 6.3                      | 0.138   |
| Race (%)                      |                    |                                 | 0.657   |
| Caucasian                     | 766 (70.9)         | 104 (73.8)                      |         |
| African American              | 304 (28.1)         | 37 (26.2)                       |         |
| Asian                         | 7 (0.6)            | 0 (0.0)                         |         |
| Current or former smoker (%)  | 518 (46.1)         | 59 (39.9)                       | 0.161   |
| Hypertension (%)              | 841 (75.0)         | 115 (77.7)                      | 0.543   |
| Dyslipidemia (%)              | 828 (74.1)         | 111 (75.0)                      | 0.920   |
| Diabetes mellitus (%)         | 363 (32.3)         | 48 (32.4)                       | 1.000   |
| Family history of coronary artery disease (%) | 260 (23.1)     | 20 (13.5)                       | 0.008   |
| Prior myocardial infarction (%) | 324 (28.8)      | 50 (33.8)                       | 0.214   |
| Prior percutaneous coronary intervention (%) | 227 (20.2)     | 39 (26.4)                       | 0.086   |
| Prior coronary artery bypass grafting (%) | 51 (4.5)        | 10 (6.8)                        | 0.222   |
| Heart failure (%)             | 139 (12.4)         | 29 (19.6)                       | 0.020   |
| Valve surgery (%)             | 8 (0.7)            | 5 (3.4)                         | 0.012   |
| Cerebrovascular disease (%)   | 126 (11.2)         | 30 (20.3)                       | 0.003   |
| Peripheral arterial disease (%) | 96 (8.5)         | 23 (15.5)                       | 0.010   |
| Chronic kidney disease (%)    |                    |                                 | 0.004   |
| GFR > 60 mL/min/1.73 m²       | 780 (77.6)         | 85 (64.4)                       |         |
| GFR 30–60 mL/min/1.73 m²      | 192 (19.1)         | 37 (28.0)                       |         |
| GFR < 30 mL/min/1.73 m²       | 19 (1.9)           | 4 (3.0)                         |         |
| Hemodialysis                  | 13 (1.3)           | 6 (4.5)                         |         |
| Chronic lung disease (%)      | 135 (12.0)         | 18 (12.2)                       | 1.000   |
| **Presentation**              |                    |                                 |         |
| Heart rate (beats per minute) | 83 [72, 96]        | 86 [71, 100]                    | 0.311   |
| Systolic blood pressure (mmHg) | 141.5 ± 26.9      | 124.9 ± 32.5                    | <0.001  |
| Cardiogenic Shock (%)         | 66 (5.9)           | 71 (48.0)                       | <0.001  |
| Creatinine (mg/dL)            | 1.0 [0.8, 1.2]     | 1.1 [0.9, 1.3]                  | <0.001  |
| Hemoglobin (g/dL)             | 14.4 ± 2.0         | 13.7 ± 2.4                      | 0.003   |
| Door-to-balloon time (minutes) | 96.5 [74, 121]    | 106 [83, 139]                   | 0.003   |
| **Angiographic findings**     |                    |                                 | 0.041   |
| Culprit vessel (%)            |                    |                                 |         |

(continued on next page)
Table 1 (continued)

| Patients with ST-elevation myocardial infarction | No cardiac arrest (N = 1124) | Cardiac arrest (N = 148) | p-Value |
|------------------------------------------------|-----------------------------|--------------------------|---------|
| Left main or left anterior descending           | 466 (41.5)                  | 77 (52.0)                |         |
| Left circumflex                                 | 209 (18.6)                  | 23 (15.6)                |         |
| Right coronary                                  | 449 (39.9)                  | 48 (32.7)                |         |
| Coronary artery dominance (%)                  |                             |                          | 0.607   |
| Right dominance                                 | 964 (85.8)                  | 123 (83.1)               |         |
| Left dominance                                  | 110 (9.8)                   | 16 (10.8)                |         |
| Co-dominance                                    | 50 (4.4)                    | 9 (6.1)                  |         |
| Saphenous vein graft conduit (%)                | 17 (1.5)                    | 3 (2.0)                  | 0.903   |
| Initial TIMI flow (%)                           |                             |                          | 0.003   |
| 0                                               | 723 (64.3)                  | 105 (70.9)               |         |
| 1                                               | 333 (29.6)                  | 29 (19.6)                |         |
| 2                                               | 36 (3.2)                    | 3 (2.0)                  |         |
| 3                                               | 32 (2.8)                    | 11 (7.4)                 |         |
| Lesion characteristic (%)                       |                             |                          | 0.924   |
| B1                                              | 34 (3.3)                    | 4 (2.9)                  |         |
| B2                                              | 339 (32.8)                  | 44 (31.7)                |         |
| C                                               | 661 (63.9)                  | 91 (65.5)                |         |
| Mechanism (%)                                   |                             |                          | 0.084   |
| Thrombus                                        | 967 (86.0)                  | 114 (77.6)               |         |
| In-stent thrombosis                             | 98 (8.7)                    | 22 (15.0)                |         |
| Chronic total occlusion                         | 25 (2.2)                    | 5 (3.4)                  |         |
| Dissection                                      | 10 (0.9)                    | 1 (0.7)                  |         |
| Embolism                                        | 24 (2.1)                    | 5 (3.4)                  |         |
| Culprit vessel size (mm)                        | 3.25 [3.0, 3.5]             | 3.5 [3.0, 3.5]           |         |
| Lesion length (mm)                              | 23 [16, 32]                 | 23 [16, 32]              | 0.796   |
| Drug-eluting stent (%)                          | 739 (75.0)                  | 71 (58.7)                | <0.001  |
| Final TIMI flow (%)                             |                             |                          | 0.425   |
| 0                                               | 19 (1.7)                    | 4 (2.7)                  |         |
| 1                                               | 11 (1.0)                    | 1 (0.7)                  |         |
| 2                                               | 31 (2.8)                    | 7 (4.8)                  |         |
| 3                                               | 1062 (94.6)                 | 134 (91.8)               |         |
| Fluoroscopy time (minutes)                      | 17.3 [12.1, 24.7]           | 18.5 [13.6, 28.1]        | 0.015   |
| Fluoroscopy dose (mGy)                          | 1418 [895, 2218]            | 1371 [819, 2264]         | 0.843   |
| Contrast volume (mL)                            | 165 [130, 213]              | 160 [126, 225]           | 0.838   |

[7.19, 7.34]) and elevated lactate (3.2[1.9, 5.7]). Compared to patients without CA, patients with STEMI and CA had a lower systolic blood pressure and were more likely to be in cardiogenic shock (48.0% vs. 5.9%, p < 0.001) with a significantly worse admission creatinine and hemoglobin (Table 1).

Angiographically, there was a greater incidence of left main or left anterior descending culprit vessel and initial TIMI 0 flow among patients with CA (Table 1). There were otherwise no differences in lesion characteristics, mechanism of STEMI, culprit vessel size, or lesion length. While fluoroscopy time was greater, there were no differences in fluoroscopy dose or contrast volume administered.

**Predictors of STEMI complicated by cardiac arrest**

When adjusting for significant characteristics in a multivariable regression model, male gender (OR: 1.69, 95% CI: 1.13–2.54, p = 0.011), chronic kidney disease (OR: 2.31, 95% CI: 1.58–3.37, p < 0.001), cerebrovascular disease (OR: 1.72, 95% CI: 1.06–2.80, p = 0.028), in-hospital STEMI (OR: 2.71, 95% CI: 1.43–5.14, p = 0.002), left main or left anterior descending culprit vessel (OR: 1.55, 95% CI: 1.09–2.21, p = 0.016), and initial TIMI 0 or 1 flow (OR: 1.50, 95% CI: 1.01–2.23, p = 0.046) were independent predictors for CA (Fig. 1; Table 2).
In-hospital care and management

Use of aspirin, an anticoagulant including heparin or bivalirudin, or glycoprotein IIb/IIIa inhibitor was similar between patients with and without CA; patients with CA were significantly less likely to receive a P2Y12 inhibitor (Fig. 2). Door-to-balloon time was significantly greater (106 [83, 139] vs. 96 [74, 121] minutes, p = 0.003) with significantly less usage of trans-radial access for PCI and greater need for mechanical circulatory support. Use of drug-eluting stents was significantly less among patients with CA (58.7% vs. 75.0%, p < 0.001). Over time, disparities in P2Y12 inhibitor usage dissipated. While door-to-balloon time and trans-radial access for PCI improved over time in both patients with and without CA, significant differences between groups persisted.

Among CA patients, 94 (63.5%) required mechanical ventilation, 29 (19.6%) required targeted temperature management, and 54 (36.5%) required vasopressors upon admission. Post-PCI, patients with CA had worse creatinine and hemoglobin and greater infarct size

| Variable                                         | Odds ratio | 95% confidence interval | p-Value |
|--------------------------------------------------|------------|-------------------------|---------|
| Male gender                                      | 1.69       | (1.13, 2.54)            | 0.011   |
| Chronic kidney disease                          | 2.31       | (1.58, 3.37)            | -0.001  |
| Cerebrovascular disease                         | 1.72       | (1.06, 2.80)            | 0.028   |
| Peripheral artery disease                       | 1.46       | (0.84, 2.51)            | 0.177   |
| Left main or left anterior descending culprit vessel | 1.55       | (1.09, 2.21)            | 0.016   |
| In-hospital presentation                        | 2.71       | (1.43, 5.14)            | 0.002   |
| In-stent thrombosis                             | 1.42       | (0.84, 2.40)            | 0.189   |
| Initial TIMI 0 or 1 flow                        | 1.50       | (1.01, 2.23)            | 0.046   |
Table 3 – In-hospital outcomes and discharge characteristics of STEMI patients with and without cardiac arrest.

| In-hospital outcomes | No cardiac arrest (N = 1124) | Cardiac arrest (N = 148) | p-Value |
|----------------------|-------------------------------|--------------------------|---------|
| Post-PCI creatinine (mg/dL) | 1.0 [0.9, 1.3] | 1.2 [0.9, 1.7] | <0.001 |
| Post-PCI hemoglobin (g/dL) | 12.2 ± 2.1 | 10.7 ± 2.4 | <0.001 |
| Post-PCI troponin T (ng/mL) | 3.6 [1.5, 6.8] | 4.0 [1.7, 8.7] | 0.106 |
| Post-PCI creatine kinase-MB (ng/mL) | 111 [43, 205] | 161 [50, 257] | 0.009 |
| Recurrent myocardial infarction (%) | 17 (1.5) | 4 (2.7) | 0.295 |
| Cerebrovascular accident (%) | 10 (0.9) | 1 (0.7) | 1.000 |
| Access site-related (%) | 106 (9.4) | 37 (25.0) | <0.001 |
| Discharge characteristics | | | |
| Ejection fraction | 48.0 ± 11.6 | 46.1 ± 13.5 | 0.066 |
| Ejection fraction <35% (%) | 198 (17.6) | 42 (28.4) | <0.001 |
| Length of stay (days) | 3 [2, 4] | 6 [3, 15] | <0.001 |
| Discharge destination (%) | | | |
| Home | 1012 (83.6) | 96 (76.2) | <0.001 |
| Acute rehabilitation | 5 (0.5) | 1 (0.8) | |
| Skilled nursing facility | 55 (5.1) | 27 (21.4) | |
| Against medical advice | 7 (0.6) | 0 (0.0) | |

Fig. 3 – Discharge therapies for STEMI patients with and without cardiac arrest.

(creatine kinase-MB 111 [43, 205] vs. 161 [50, 257] ng/dL, p = 0.009) and major bleeding (25.0% vs. 9.4%, p < 0.001) (Table 3).

Hospitalization length of stay was significantly longer among patients with STEMI and CA (Table 3). There was a greater incidence of severe left ventricular dysfunction with ejection fraction <35% (28.4% vs. 17.6%, p = 0.002). Upon discharge, there were similar rates of prescription for aspirin, P2Y12 inhibitor, angiotensin converting enzyme inhibitor or angiotensin receptor antagonist, and beta-blocker (Fig. 3), but not statins (92.9% vs. 97.8%, p = 0.005). Patients with CA were less likely to be discharged home (76.2% vs. 93.6%, p < 0.001) with a significant need for post-discharge rehabilitation.

**Short-term outcomes**

Thirty-day mortality was greater among patients with STEMI and CA (16.2% vs. 4.1%, p < 0.001). Differences and absolute rates of mortality remained stable among groups over time. Among patients with CA, significantly greater mortality was demonstrated in those with concomitant cardiogenic shock (23.9% vs 9.1%, p = 0.014), prolonged cardiopulmonary resuscitation >5 min (32.7% vs. 7.3%, p < 0.001), or cerebral performance category of 4 (48.6% vs. 6.2%, p < 0.001). In univariable logistic regression analysis, body mass index, age, male gender, door-to-balloon time, baseline chronic kidney disease, diabetes mellitus, ejection fraction <35%, cardiogenic shock on presentation, non-shockable rhythm of pulseless electrical activity or asystole, prolonged cardiopulmonary resuscitation >5 min, cerebral performance category of 4 on presentation, serum pH, and need for mechanical ventilation upon admission were significant predictors for 30-day mortality among CA patients (Table 4).

In ROC analysis, cut-points for the continuous variables were chosen as follows: body mass index <22.3 kg/m², age >63.7 years, door-to-balloon time >104.5 min, serum pH < 7.26. An ROC curve constructed using all variables displayed an area under the curve (AUC) of 0.931 with a sensitivity of 82.6% and specificity of 92.4% (Fig. 4A). To create a predictive risk score for 30-day mortality, each variable was given a value based on weighted odds ratios (Table 4). An ROC curve constructed using this risk score displayed an AUC of 0.902 (95% CI: 0.843–0.960) with a sensitivity of 83.3% and specificity of 83.1% (Fig. 4B). A breakdown of patients by risk score and mortality is shown in Supplemental Table 1. In comparison, the CathPCI Risk Score System displayed an AUC of 0.688 (95% CI: 0.572–0.803) with a sensitivity of 75.0% and specificity of 56.5%.
Long-term outcomes

Patients with STEMI and CA had a significantly greater 1-year (22.2% vs. 8.8%, p < 0.001) and long-term (p < 0.001, Fig. 5A) mortality compared to STEMI patients without CA. However, when comparing those who survived to hospital discharge, this difference dissipated over 1-year (7.4% vs. 5.2%, p = 0.301) and long-term follow-up of 4.5 ± 2.4 years (p = 0.064, Fig. 5B). In multivariable Cox regression

| Variable                                      | Odds ratio | 95% confidence interval | p-Value | Cut-point | Value |
|-----------------------------------------------|------------|-------------------------|---------|-----------|-------|
| Body mass index (kg/m²)                       | 0.92       | (0.85, 1.01)            | 0.068   | <22.3     | 1     |
| Age (per year)                                | 1.03       | (0.99, 1.07)            | 0.076   | >63.7     | 1     |
| Female gender                                 | 5.16       | (2.17, 14.3)            | <0.001  | NA        | 5     |
| Door-to-balloon time (per minute)             | 1.01       | (1.0, 1.02)             | 0.013   | >104.5    | 1     |
| Chronic kidney disease                        | 6.05       | (2.2, 16.6)             | <0.001  | NA        | 6     |
| Diabetes mellitus                             | 3.73       | (1.48, 9.38)            | 0.005   | NA        | 4     |
| Ejection fraction <35%                        | 4.29       | (1.69, 10.9)            | 0.002   | NA        | 4     |
| Cardiogenic shock                             | 2.91       | (1.11, 7.61)            | 0.029   | NA        | 3     |
| Non-shockable rhythm                          | 4.76       | (1.47, 15.4)            | 0.009   | NA        | 5     |
| Cardiopulmonary resuscitation >5 Min         | 6.27       | (2.36, 16.7)            | <0.001  | NA        | 6     |
| Cerebral performance category 4 on admission  | 14.3       | (5.1, 40.1)             | <0.001  | NA        | 14    |
| Serum pH (per 0.10)                           | 0.21       | (0.02, 0.4)             | <0.001  | <7.26     | 5     |
| Mechanical ventilation on admission           | 4.71       | (1.32, 16.7)            | 0.017   | NA        | 5     |
| Total risk score                              |            |                        |         | 60        |       |

Fig. 4 – ROC curve fitted to the multivariable analysis of (A) important variables which predict 30-day mortality among patients with STEMI and cardiac arrest and (B) 30-day mortality risk score created using weighted odds ratios.
analysis, there was no association between CA and mortality among those that survived to hospital discharge (HR 1.01, 95% CI: 0.56 –1.82, p = 0.969). Instead, independent predictors for long-term mortality among STEMI patients surviving to hospital discharge included cardiogenic shock during index hospitalization, African American race, increasing age, chronic kidney disease, peripheral arterial disease, and reduction in ejection fraction while use of guideline-directed medical therapy (aspirin, P2Y12 inhibitor, beta-blocker, and statin) was protective (Table 5).

Discussion

In this analysis, we found that CA complicating STEMI occurred in almost one-in-eight patients undergoing primary PCI. Patients with STEMI and CA had more comorbidities with in-hospital presentation, chronic kidney disease, cerebrovascular disease, and male gender important predictors for CA. While these patients were more likely to present with cardiogenic shock, they were less likely to receive guideline-recommended therapies. They had longer hospitalizations with worse in-hospital outcomes, including infarct size and major bleeding. Despite accounting for only 11.6% of all patients in this sample, they accounted for more than one-third of the overall in-hospital and 30-day mortality. Prognosis was driven by numerous factors including baseline comorbidities, age, and gender with particular emphasis on concomitant cardiogenic shock, features of the arrest, and neurologic status. However, among patients with STEMI and CA that survived to hospital discharge, there were no significant differences in long-term mortality.

Table 5 – Landmark analysis of predictors for long-term survival among patients with STEMI who survive to hospital discharge.

| Variable                                | Odds ratio | 95% confidence interval | p-Value |
|-----------------------------------------|------------|-------------------------|---------|
| Cardiac arrest                          | 1.01       | (0.56, 1.82)            | 0.969   |
| Cardiogenic shock                       | 1.90       | (1.06, 3.40)            | 0.031   |
| African American race                   | 1.74       | (1.19, 2.55)            | 0.004   |
| Body mass index (kg/m²)                 | 0.98       | (0.95, 1.01)            | 0.113   |
| Age (year)                              | 1.03       | (1.02, 1.05)            | <0.001  |
| Male gender                             | 0.73       | (0.51, 1.05)            | 0.087   |
| Chronic kidney disease                  | 1.99       | (1.35, 2.93)            | <0.001  |
| Peripheral artery disease               | 2.21       | (1.39, 3.53)            | <0.001  |
| Ejection fraction (%)                   | 0.97       | (0.96, 0.98)            | <0.001  |
| Cardiac rehabilitation referral         | 0.73       | (0.49, 1.07)            | 0.106   |
| Guideline-directed medical therapy      | 0.51       | (0.31, 0.84)            | 0.008   |
| Drug-eluting stent                      | 0.70       | (0.48, 1.03)            | 0.071   |
First, amongst STEMI patients who undergo PCI, the risk associated with CA seems to be largely upfront during the index hospitalization with those surviving to hospital discharge having similar long-term mortality to patients without CA. Our findings are consistent with a recently published study describing outcomes of patients with STEMI and CA from 2003 to 2014. Our risk score, which demonstrated excellent predictive accuracy of early prognosis and outperformed the CathPCI Risk Score System, highlights the heterogeneity of STEMI-associated CA. This spectrum encompasses patients who develop a shockable rhythm and prompt return to spontaneous circulation without cardiogenic shock to those with refractory CA, concomitant cardiogenic shock, and poor neurologic outcome. Additionally, it highlights the cumulative role that baseline comorbidities, in addition to features of the CA and subsequent therapies provided, play in determining prognosis. However, whether these risks are modifiable is unclear. It remains unknown if implementation of a system of care which standardizes guideline-directed medical therapy, improves door-to-balloon times, and promotes revascularization and access to mechanical circulatory support could result in improvement in in-hospital mortality and thus translate to superior outcomes.

Concordantly, we found that patients with STEMI and CA were less likely to receive some strategies that have been proven in randomized studies to reduce mortality in STEMI, namely use of P2Y12 inhibitors and trans-radial access for PCI. This “risk-treatment paradox,” in which patients at highest risk are least likely to receive mortality reducing therapies, has previously been described in patients with acute coronary syndromes, atrial fibrillation, and in the use of trans-radial access for PCI. Importantly, different aspects of STEMI care have been shown to provide incremental prognostic value via mortality benefit and a reduction in adverse events. However, patients with STEMI and CA are often excluded from door-to-balloon time reporting due to non-system delay, a subpopulation of STEMI patients that have been shown to have increased in-hospital mortality. Whether a systems of care targeting this high-risk population can improve quality of care and outcomes remains unclear.

It is notable that in-hospital STEMI is both common and frequently complicated by CA. In this cohort, in-hospital STEMI accounted for 6.2% of the overall patient population of which 25.3% had concomitant CA. The reason why these patients are at excessive risk for CA remains unclear. In-hospital STEMI is a unique clinical entity that until recently remained undefined. It occurs more frequently in patients that are older, female, have comorbid and active disease processes, atypical symptoms resulting in a delay in diagnosis, more likely to develop bleeding complications and cardiogenic shock, and are less likely to undergo cardiac catheterization. They are frequently admitted to non-cardiac services which are less accustomed to ECG acquisition, interpretation, and STEMI activation. In-hospital mortality rates are much higher than that reported for conventional out-of-hospital STEMI. Importantly, while care processes for out-of-hospital STEMI are commonplace, few systems which promote recognition, triage, and management of in-hospital STEMI exist leading to delays in diagnosis and treatment. While implementation of quality improvement programs have been shown to improve STEMI recognition and reduce symptom-to-first device activation time, the impact on incidence of cardiac arrest, in-hospital mortality, and long-term mortality remains to be seen.

**Limitations**

Although this analysis provides granular insight into the contemporary presentation, management, and outcomes of patients with STEMI and CA, there are several limitations to acknowledge. Namely, this is a single center study including STEMI patients who survived to cardiac catheterization laboratory arrival and underwent attempted PCI. As such, our findings are subject to the inherent limitations of a single center study and do not reflect characteristics of STEMI patients who were deemed not candidates for PCI (neurologic devastation, prolonged arrest without return of spontaneous circulation, etc.). However, our intent was to capture a “real world” description of these patients in whom PCI may be considered rather than those in whom PCI is likely futile. Next, while our risk score predicting 30-day mortality among patients with CA had excellent prognostic accuracy, external validation is warranted and requires further study. Lastly, we did not have access to pre-hospital treatments among the CA patients which may have yield important information regarding prognostication and outcomes.

**Conclusions**

Patients with STEMI and CA who undergo PCI present through every phase of presentation, supporting need for heightened vigilance across the geographic spectrum of care. A large proportion of patients with in-hospital STEMI develop CA, highlighting an important mechanism of their increased mortality rate. Patients with STEMI and CA have greater comorbidities with those who have kidney dysfunction, male gender, and cerebrovascular disease being particularly at risk for CA. CA is associated with significantly higher morbidity and mortality compared with STEMI without CA, and use of readily available baseline and presenting characteristics can provide excellent prognostic accuracy for predicting 30-day mortality. However, CA carries no long-term mortality risk among those who survive to hospital discharge. Strategies to improve in-hospital care and outcomes of STEMI patients with CA are needed.

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**Conflicts of interest**

None.

**CRediT authorship contribution statement**

A Kumar: Dr. Kumar had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the
data analysis. Dr. Kumar contributed to the conception and design of the study, the data analysis, the data interpretation, the manuscript drafting, and the critical revision of the manuscript.

L Zhou: Dr. Zhou contributed to the design of study, the data analysis, the data interpretation, and the critical revision of the manuscript.

CP Huded: Dr. Huded contributed to the design of study, the data analysis, the data interpretation, and the critical revision of the manuscript.

LA Moennich: Ms. Moennich contributed to the design of study, the data analysis, the data interpretation, and the critical revision of the manuscript.

V Menon: Dr. Menon contributed to the data interpretation and the critical revision of the manuscript.

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UN Khot: Dr. Khot contributed to the conception and design of the study, the supervision, the data analysis, the data interpretation, the manuscript drafting, and the critical revision of the manuscript. Dr. Khot is the corresponding author.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resplu.2021.100149.

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