ORIGINAL RESEARCH

Incidence and Predictors of Adverse Events Among Initially Stable ST-Elevation Myocardial Infarction Patients Following Primary Percutaneous Coronary Intervention

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BACKGROUND: Cardiac intensive care units were originally created in the prerevascularization era for the early recognition of ventricular arrhythmias following a myocardial infarction. Many patients with stable ST-segment–elevation myocardial infarction (STEMI) are still routinely triaged to cardiac intensive care units after a primary percutaneous coronary intervention (pPCI), independent of clinical risk or the provision of critical care therapies. The aim of this study was to determine factors associated with in-hospital adverse events in a hemodynamically stable, postreperfusion population of patients with STEMI.

METHODS AND RESULTS: Between April 2012 and November 2019, 2101 consecutive patients with STEMI who received pPCI in the Vancouver Coastal Health Authority were evaluated. Patients were stratified into those with and without subsequent adverse events, which were defined as cardiogenic shock, in-hospital cardiac arrest, stroke, re-infarction, and death. Multivariable logistic regression models were used to determine predictors of adverse events. After excluding patients presenting with cardiac arrest, cardiogenic shock, or heart failure, the final analysis cohort comprised 1770 stable patients with STEMI who had received pPCI. A total of 94 (5.3%) patients developed at least one adverse event: cardiogenic shock 55 (3.1%), in-hospital cardiac arrest 42 (2.4%), death 28 (1.6%), stroke 21 (1.2%), and re-infarction 5 (0.3%). Univariable predictors of adverse events were older age, female sex, prior stroke, chronic kidney disease, and atrial fibrillation. There was no significant difference in reperfusion times between those with and without adverse events. Following multivariable adjustment, moderate to severe chronic kidney disease (creatinine clearance <44 mL/min; 13% of cohort) was associated with adverse events (odds ratio 2.24 [95% CI, 1.12–4.48]) independent of reperfusion time, age, sex, smoking status, hypertension, diabetes, and prior myocardial infarction/PCI/coronary artery bypass grafting.

CONCLUSIONS: Only 1 in 20 initially stable patients with STEMI receiving pPCI developed an in-hospital adverse event. Moderate to severe chronic kidney disease independently predicted the risk of future adverse events. These results indicate that the majority of patients with STEMI who receive pPCI may not require routine admission to a cardiac intensive care unit following reperfusion.

Key Words: creatine ■ heart failure ■ myocardial infarction ■ percutaneous coronary intervention ■ shock, cardiogenic ■ ST-elevation myocardial infarction

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The development and widespread implementation of cardiac intensive care units (CICUs) for the care of patients with ST-segment–elevation myocardial infarction (STEMI) was primarily driven by the early recognition and treatment of ventricular arrhythmias in an era before the utilization of primary percutaneous coronary intervention (pPCI).1–5 Advances in STEMI reperfusion systems have considerably reduced cardiovascular complications in patients with acute coronary syndromes.6–9 However, in many centers it is still considered the standard of care to admit patients with STEMI to the CICU after pPCI irrespective of clinical stability on presentation despite limited contemporary data supporting this widespread practice.10,11 Recent studies have shown that despite the low risk of complications among patients with non–ST-segment–elevation myocardial infarction following pPCI, CICU admission is common. One study that analyzed 7900 non–ST-segment–elevation myocardial infarction presentations found no significant difference in clinical outcomes among those admitted to an ICU bed versus a telemetry ward bed.12,13 Another study showed that while only 14% of 29,973 patients with non–ST-segment–elevation myocardial infarction developed complications requiring ICU admission, almost half were nevertheless admitted to intensive care.14,15 Risk stratification and identification of those clinically stable patients with STEMI who may not require CICU management might optimize patient care, relieve acute care congestion, and reduce health care spending.

We evaluated consecutive, hemodynamically stable patients with STEMI who had undergone pPCI at the Vancouver Coastal Health Authority from 2012 to 2019 with the overall goal of determining the incidence and predictors of in-hospital adverse events. Previously, we have shown that non-access-site major bleeding was an independent predictor of adverse events, including mortality, among patients with STEMI undergoing pPCI.16 We hypothesized that most clinically stable patients with STEMI post pPCI do not experience an adverse event, and that baseline clinical characteristics could predict adverse outcomes.

**METHODS**

**Study Population**

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results. This study was a retrospective analysis using the Vancouver Coastal Health Authority STEMI Database (2 PCI-capable hospitals; 11 PCI noncapable hospitals), as previously described.17–19 From April 1, 2012 to November 3, 2019, data were collected prospectively on 2681 consecutive patients presenting with STEMI, and 2101 patients receiving pPCI were included. Three hundred twenty-six patients were excluded, given compelling indications for critical care including heart failure, cardiogenic shock, cardiac arrest, or unknown clinical presentation. An additional 5 patients were excluded for missing adverse event data. The final analysis population included 1770 patients admitted to a Cardiac Intensive Care Unit as is routine regional practice (Figure 1). Informed consent of subjects was not required.

**Definitions**

First medical contact was defined as the time at which a health care provider was at the patient’s side; this would be the time of triage at the first emergency department for patients who presented at the hospital without use of Emergency Medical Service transport or the time of arrival of a paramedic at the side of a patient transported to the hospital by Emergency Medical Service. Based on recent guidelines for patients with STEMI in urban centers in Canada, timely versus delayed reperfusion times was defined as reperfusion time goal of ≤90 minutes.
versus >90 minutes, respectively, for patients presenting to a PCI center, or ≤120 versus >120, respectively, for patients presenting initially to non-PCI centers. Cardiogenic shock was defined as cardiac index ≤2.2 mL/min per m² or systolic blood pressure ≤90 mm Hg persisting for >30 minutes. Heart failure was defined as the presence on admission of clinical symptoms, Killip class 2–4, or imaging evidence of pulmonary edema on admission. Pre-PCI cardiac arrest was defined as ventricular tachycardia, ventricular fibrillation, pulseless electric activity, or asystole requiring advanced cardiac life support management before pPCI. A stable patient with STEMI was defined as one who had no evidence of heart failure, cardiogenic shock, or cardiac arrest on initial presentation or in the Cath Lab. Adverse events were defined as in-hospital re-infarction, stroke, cardiogenic shock, cardiac arrest, and all-cause mortality. Moderate to severe chronic kidney disease (CKD) was defined as creatine clearance <45 mL/min. Major bleeding was defined by an overt bleeding event that requires transfusion of whole blood, packed red blood cells, or use of a surgical or procedural intervention to manage the bleeding, or is associated with a hemoglobin reduction of at least 30 g/L. Access-site major bleed included any major bleed originating from the femoral or radial arterial puncture site. Retroperitoneal bleeds were categorized as access-site bleeding if the participant had a femoral arterial puncture for pPCI access. Non-access-site major bleed included all other major bleeds.

### Statistical Analysis

All data were analyzed with Statistical Analysis System (SAS) software version 9.4 (SAS Institute, Cary, NC). Patients who did or did not develop adverse events were compared using the t test or Wilcoxon rank sum test for continuous variables and the χ² or Fisher exact test for categorical variables as appropriate. Continuous variables were calculated as medians with interquartile range or means±SDs, and categorical variables as percentages. A multivariable logistic regression model was used to assess the association between the development of adverse events and clinical characteristics. The model included the following clinical characteristics considered to be of possible prognostic significance: renal function status, first medical contact-to-device time, age, sex, smoking status, hypertension, diabetes, prior myocardial infarction, PCI, or coronary artery bypass graft. Firth’s penalized likelihood approach was used because of low count for some of the binary predictor variables. Results were presented as odds ratio (OR). Variance inflation factor was used to detect multicollinearity among the predictor variables. Because of a limited number of adverse events in this cohort and to minimize the possibility of overfitting, we performed a sensitivity analysis for which the multivariable model included only the aforementioned parameters that have a P value of ≤0.2 in the univariate analysis. Statistical significance was determined as a P value of ≤0.05. This study was approved by the clinical research ethics board of the University of British Columbia.

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**Figure 1.** Cohort derivation.

PCI indicates percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and VCHA, Vancouver Coastal Health Authority.
RESULTS
Baseline Patient Demographics
The mean age of the study population was 65.4 years with body mass index of 26.8. Patients were predominantly male (80.2%) and nonsmokers (76.3%). There was a history of hypertension in 57.4%, dyslipidemia in 45.5%, CKD in 27.4%, diabetes in 20.9%, stroke in 7.6%, previous myocardial infarction in 14.9%, previous revascularization in 14.6% (12.3% PCI, 2.3% coronary artery bypass graft), and new onset or history of atrial fibrillation in 10.9%. The proportion of patients with an anterior STEMI was 46.7% (n=826), among whom 6.3% (n=52) were in the adverse event cohort. Adverse events were more common in older patients. Patients with adverse events were older (mean age 70.4 versus

Table 1. Patient Demographics and Clinical Characteristics of Studied Cohort

| Variables                        | Study population | Any adverse events | P value‡ |
|----------------------------------|------------------|--------------------|----------|
| Mean age, y (SD)                 | n=1770           | No (n=1676)        | Yes (n=94) |
|                                  | 65.4 (12.5)      | 65.1 (12.3)        | 70.4 (14.3) | <0.001 |
| Mean BMI, (SD)*                  | 26.8 (4.9)       | 26.8 (4.9)         | 26.7 (4.5)  | 0.892  |
| Sex, n (%)                       |                  |                    |           |
| Female                           | 351 (19.8)       | 321 (19.2)         | 30 (31.9) | 0.003  |
| Male                             | 1419 (80.2)      | 1355 (80.8)        | 64 (68.1) |        |
| Current/recent smoker, n (%)*    | 419 (23.7)       | 397 (23.7)         | 22 (23.4) | 0.947  |
| Recent cocaine use, n (%)*       | 31 (1.8)         | 30 (1.8)           | 1 (1.1)   | 0.599  |
| Dyslipidemia, n (%)              | 788 (44.5)       | 744 (44.4)         | 44 (46.8) | 0.646  |
| Hypertension, n (%)              | 1016 (57.4)      | 959 (57.2)         | 57 (60.6) | 0.514  |
| Currently on dialysis, n (%)     | 6 (0.3)          | 6 (0.4)            | 0 (0.0)   | 1.000  |
| Diabetes, n (%)*                 | 370 (20.9)       | 356 (21.2)         | 14 (15.1) | 0.153  |
| Prior MI, n (%)                  | 264 (14.9)       | 247 (14.7)         | 17 (18.1) | 0.375  |
| Prior heart failure, n (%)*      | 34 (1.9)         | 29 (1.7)           | 5 (5.3)   | 0.014  |
| Prior PCI, n (%)                 | 218 (12.3)       | 204 (12.2)         | 14 (14.9) | 0.435  |
| Prior CABG, n (%)                | 40 (2.3)         | 38 (2.3)           | 2 (2.1)   | 0.929  |
| Prior TIA/CVA, n (%)             | 135 (7.6)        | 116 (6.9)          | 19 (20.2) | <0.001 |
| Prior PVD, n (%)*                | 47 (2.7)         | 43 (2.6)           | 4 (4.3)   | 0.322  |
| History of or new-onset atrial fibrillation, n (%) | 828 | 797 | 31 | <0.001 |
| Unknown                          |                  |                    |           |
| New onset                       | 42 (4.5)         | 33 (3.8)           | 9 (14.3)  |        |
| No                               | 840 (92.2)       | 795 (90.4)         | 45 (71.4) |        |
| Paroxysmal                       | 13 (1.4)         | 13 (1.5)           | 0 (0.0)   |        |
| Prior                            | 47 (5.0)         | 38 (4.3)           | 9 (14.3)  |        |
| Initial mean HR, bpm (SD)        | 76.9 (20.9)      | 76.6 (20.8)        | 80.9 (23.5)| 0.054 |
| Initial mean SBP, mmHg (SD)      | 143.4 (31.3)     | 144.1 (31.1)       | 131.3 (32.8)| <0.001 |
| Initial mean creatinine, mmol/L* | 96.9 (46.3)      | 96.7 (47.2)        | 100.6 (26.9)| 0.012 |
| Chronic kidney disease*          | 143.4 (38.2)     | 143.6 (39.0)       | 139.3 (15.7)| 0.038 |
| No (CrCl: ≥60)                   | 1280 (72.6)      | 1228 (73.6)        | 52 (55.9) | <0.001 |
| Mild (CrCl: 45–59)               | 257 (14.6)       | 242 (14.5)         | 15 (16.1) |        |
| Moderate (CrCl: 30–44)           | 161 (9.1)        | 142 (8.5)          | 19 (20.4) |        |
| Severe (CrCl: <30)               | 64 (3.6)         | 57 (3.4)           | 7 (7.5)   |        |
| Infarct type, n (%)              | 826 (46.7)       | 774 (46.2)         | 52 (55.3) | 0.084  |
| Anterior                         | 944 (53.3)       | 902 (53.8)         | 42 (44.7) |        |

New-onset atrial fibrillation indicates patients who were not previously known to have atrial fibrillation but subsequently developed atrial fibrillation while in the hospital. BMI indicates body mass index; bpm, beats per minute; CABG, coronary artery bypass grafting; CrCl, creatinine clearance; CVA, cerebrovascular accident; Hg, hemoglobin; HR, heart rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, Peripheral Vascular Disease; SBP, systolic blood pressure; and TIA, transient ischemic attack.

*Data missing for up to 8 patients.

†Cockcroft-Gault CrCl, mL/min=(140– age)/(weight, kg×(0.85 if female)/(72×Cr, mg/dL).

‡P value was based on χ² test, Fisher exact test, t test, or Wilcoxon rank sum test as appropriate.

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and there were proportionately more adverse events among female patients than males (9% versus 5%) (Table 1).

Reperfusion Times
Among patients with STEMI receiving pPCI with known reperfusion times (n=1768), there was no significant difference in the incidence of adverse events among patients with timely (n=36/853; 2.0%) versus delayed (n=57/915; 3.2%) reperfusion ($P$=0.059). The median Vancouver Coastal Health Authority first medical contact-to-device time was 102 minutes (94 minutes for PCI-capable versus 120 for non-PCI-capable hospitals) (Table 2). After adjustment, there was no statistically significant association between reperfusion time and adverse events (OR, 1.3 [95% CI, 0.84–2.00]) (Figure 2).

In-Hospital Major Bleeding Events
Of the 1770 stable patients with STEMI who received pPCI, 123 (7%) had a major in-hospital bleeding event. Access site bleeding event constituted 69/123 (3.9%) of which 9 patients (9.6%) had an adverse event versus nonaccess site 54/123 (3.1%) of which 23 patients (24.5%) had an adverse event.

In-Hospital Adverse Events
Of the 1770 stable patients with STEMI who received pPCI, 94 (5.3%) had at least one adverse event. Individual adverse events occurred in the following numbers and frequencies: cardiogenic shock 55 (3.1%), in-hospital cardiac arrest 42 (2.4%), stroke 21 (1.2%), reinfarction 5 (0.3%), and death 28 (1.6%); 32 patients had >1 adverse event (Table 3). Moreover, the median hospital length of stay was 2.9 days (IQR, 2.3–3.5) and median time to death was 5.8 days (0.9–16.0).

Predictors of In-Hospital Adverse Events
After multivariable adjustment, the only clinical factor that was associated with an increased likelihood of developing an adverse event was moderate to severe CKD (OR, 2.24 [95% CI, 1.12–4.48]) (Figure 2). The variance inflation factor was <2 for all predictors, consistent with minimal collinearity among the predictors. Our conclusion remained unchanged in the sensitivity analysis for which the multivariable model included

Table 2. FMC-to-Device Times Among Patients With Adverse Events Versus Those With No Adverse Events in PCI-Capable and Non-Capable Hospitals

| Variables                                           | Study population | Any adverse events | $P$ value† |
|-----------------------------------------------------|------------------|--------------------|------------|
|                                                     | No               | Yes                |            |
| FMC-to-device, n (%)*                      | 853 (48.2)       | 817 (48.8)         | 0.059      |
| ≤90 (or 120) min                                 | 915 (51.8)       | 858 (51.2)         | 0.112      |
| >90 (or 120) min                                 | 1768             | 1675               | 93         |
| Median (IQR)                                     | 102 (85, 130)    | 102 (85, 129)      | 0.067      |
| Mean (SD)                                         | 114.9 (51.2)     | 114.5 (51.1)       |            |
| Range                                             | (39, 736)        | (39.0, 736.0)      |            |
| FMC-to-device (minutes; among those presented to PCI-capable hospital)* | 1198             | 1134               | 64         |
| Median (IQR)                                     | 94 (79, 118)     | 94 (78, 117)       |            |
| Mean (SD)                                         | 104.8 (44.5)     | 104.3 (44.2)       |            |
| Range                                             | (39, 337)        | (39, 337)          |            |
| FMC-to-device (minutes; among those presented to PCI noncapable hospital) | 570              | 541                | 0.535      |
| Median (IQR)                                     | 120 (102, 151)   | 119 (102, 150)     |            |
| Mean (SD)                                         | 136.2 (57.4)     | 136.0 (57.7)       |            |
| Range                                             | (68, 736)        | (72, 736)          |            |

Among 1770 Patients, 1200 and 570 Were Presented to PCI-Capable Hospitals and PCI Non-Capable Hospitals, Respectively. FMC indicates first medical contact; IQR, interquartile range; and PCI, percutaneous coronary intervention.

*Data missing for 2 patients.
†$P$ value was based on $\chi^2$ test, Fisher exact test, t test, or Wilcoxon rank sum test as appropriate.
only age, sex, CKD, and reperfusion time as predictors (those with \( P < 0.2 \) in the univariate analysis). In particular, only moderate to severe CKD (OR, 2.18 [95% CI, 1.10–4.33]) was associated with an adverse event.

### DISCUSSION

In this contemporary population-based analysis of consecutive patients with STEMI who were clinically stable following pPCI, 5.3% experienced adverse events justifying CICU care. The only independent predictor of in-hospital adverse events was moderate to severe CKD, which was present in 13% of the study cohort. These results support the use of a risk-based triage model to enhance routine CICU utilization among stable patients with STEMI.

Historically, patients with STEMI were admitted to CICU for ventricular arrhythmia monitoring and outcomes were greatly improved.\(^{20,21}\) The widespread use of contemporary pPCI has reduced the risk of adverse cardiovascular events.\(^{6–9}\) Early identification of low-risk patients with myocardial infarction for bypassing CICU have been done but to our knowledge, only 1 previous large contemporary study has explored the apparent disparity between persistently high CICU utilization and the currently low risk of complications among patients with STEMI.\(^{11,22}\) This analysis confirms the relatively low rate of CICU complications in a stable STEMI cohort and extends these findings by showing that significant CKD remains an independent predictor of adverse events. Our findings did not demonstrate that reperfusion delays were independently associated with adverse events in this more selected stable STEMI population. In contrast to the above study, the current study was based on a single regional health system with 2 PCI centers where all patients with STEMI were triaged to CICU. Age was not an exclusion criterion, and different but important criteria were used for defining unstable patients, such as any evidence of heart failure independent of shock. These factors may have selected against those patients who would have otherwise shown reperfusion delay as an independent factor for post pPCI complications among initially stable patients with STEMI. This suggests that among stable patients with STEMI, comorbidities may better predict early outcomes following revascularization, independent of reperfusion delays. This is germane to clinical care since comorbidities are readily discernable to improve risk assessment and triage of this initially stable STEMI cohort.

In North America, although a large proportion (up to 80%) of patients with STEMI are admitted to CICUs, there are limited data or guidance supporting this ongoing practice.\(^{23}\) Instead, recent studies have focused on assessing hemodynamically stable patients with non–ST-segment–elevation myocardial infarction
undergoing uncomplicated pPCI, perhaps related to the heterogeneity of this population.\textsuperscript{24–28} Yet, the routine admission of stable patients with STEMI has the potential to significantly burden hospital resources and add to the growing health care costs since up to 35\% of all hospital costs are associated with critical care units despite comprising only 5\% of total hospital beds.\textsuperscript{29–31} In the STEMI population, there are several validated risk scores (eg, the Zwolle Score) available to guide clinical decision making, potentially reducing costs without compromising patient care. However, the Zwolle Score does not account for severe CKD as an independent factor for predicting adverse events.\textsuperscript{32} The Zwolle Score had enhanced discriminatory power to predict early mortality when CKD was added as an independent variable.\textsuperscript{33} The use of a risk-based triage model, which includes significant independent variables associated with adverse events, such as CKD, may prevent unnecessary costs without compromising patient outcomes, and reliably identify a large STEMI cohort post pPCI at very low risk, who may reasonably be considered for early discharge strategy.

This study has some limitations. First, there may be other clinically important factors or other adverse events that require critical care that could not be captured in this study, such as high-grade atrioventricular block, malignant arrhythmias not leading to cardiac arrest or hemodynamic instability, and respiratory failure requiring invasive or noninvasive ventilation. Second, the timing of each of the evaluated adverse events following admission or other known clinically important prognostic variables such as left ventricular systolic function before hospitalization is unknown, and could impact risk. Third, it is possible that the low rate of adverse events was related to early CICU care and rapid response to recurrent ischemia or early instability. Finally, our study is based on a regional STEMI system with 2 PCI-capable centers and multiple referral hospitals, which may not be universally applicable.

In conclusion, among a large, contemporary cohort of patients with STEMI initially stable following pPCI, only 1 in 20 developed an adverse event supporting CICU care. Moderate to severe CKD was the only clinical variable that independently predicted adverse events. These results support the use of a contemporary risk-based triage model to enhance routine CICU utilization among stable patients with STEMI, who may not routinely require critical care resources. Ongoing efforts are needed to further define those post pPCI patients likely to benefit from CICU care.

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