Coronary Heart Disease

Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease

A Report From the National Cardiovascular Data Acute Coronary Treatment and Intervention Outcomes Network Registry

Caroline S. Fox, MD, MPH; Paul Muntner, PhD, MHS; Anita Y. Chen, MS; Karen P. Alexander, MD; Matthew T. Roe, MD; Christopher P. Cannon, MD; Jorge F. Saucedo, MD; Michael C. Kontos, MD; Stephen D. Wiviott, MD

Background—Chronic kidney disease (CKD) is a risk factor for myocardial infarction (MI) and death. Our goal was to characterize the association between CKD severity and short-term outcomes and the use of in-hospital evidence-based therapies among patients with ST-segment elevation MI (STEMI) and non–ST-segment elevation MI (NSTEMI).

Methods and Results—The study sample was drawn from the Acute Coronary Treatment and Intervention Outcomes Network registry, a nationwide sample of STEMI (n=19,029) and NSTEMI (n=30,462) patients. Estimated glomerular filtration rate was calculated with the Modification of Diet in Renal Disease equation in relation to use of immediate (first 24 hours) therapies and early (first 48 hours) cardiac catheterization as well as in-hospital major bleeding events and death. Overall, 30.5% and 42.9% of patients with STEMI and NSTEMI, respectively, had CKD. Regardless of MI type, patients with progressively more severe CKD had higher rates of death. For STEMI, the odds ratio for stage 3a, 3b, 4, and 5 CKD compared with patients with no CKD was 2.49, 3.72, 4.82, and 7.97, respectively (P<0.0001). For NSTEMI, the analogous odds ratios were 1.81, 2.41, 3.50, and 4.09 (P for trend <0.0001). In addition, patients with progressively more severe CKD were less likely to receive immediate evidence-based therapies including aspirin, β-blockers, or clopidogrel, were less likely to undergo any reperfusion (STEMI) or revascularization (NSTEMI), and had higher rates of bleeding.

Conclusions—Reports over the past decade have highlighted the importance of CKD among patients with MI. Data from this contemporary cohort suggest that patients with CKD still receive fewer evidence-based therapies and have substantially higher mortality rates. (Circulation. 2010;121:357-365.)

Key Words: kidney • myocardial infarction • outcomes

Kidney disease affects 26 million adults in the United States, and nearly half a million individuals in the United States have end-stage renal disease. Chronic kidney disease (CKD) is associated with an increased risk for cardiovascular disease, stroke, peripheral arterial disease, and all-cause mortality. Hypertension, dyslipidemia, and diabetes mellitus are common among patients with CKD but are often inadequately treated in this population.

Clinical Perspective on p 365

Results from previous studies indicate that patients with CKD, and particularly those undergoing dialysis, are known to have poor outcomes after the occurrence of acute coronary syndromes. However, several of these studies have been limited to dialysis patients; and others are secondary analyses of clinical trial data with strict inclusion and exclusion criteria with respect to moderate and severe CKD. Because patients with CKD have been systematically excluded from clinical trials, the prevalence and outcomes for patients with varying degrees of CKD (particularly stages 3 to 5), patients commonly seen in clinical practice, remain unknown.
practice, have not been well studied in the post–myocardial infarction (MI) setting. As such, previous findings are of limited utility in understanding the relationship between the severity of CKD and outcomes in unselected patient populations.

Therefore, the purpose of this analysis is to characterize the short-term outcomes related to CKD in a large hospital-based registry of post-MI patients. Despite a high risk of adverse outcomes, we hypothesized that patients with CKD would be less likely to receive proven beneficial procedures and medications than their counterparts without CKD.

Methods

Study Sample

Patients for this study were drawn from the National Cardiovascular Data Registry (NCDR) Acute Coronary Treatment and Intervention Outcomes Network (ACTION) registry, a nationally representative, quality improvement registry of ST-segment elevation MI (STEMI) and non–ST-segment elevation MI (NSTEMI) that began enrolling patients January 1, 2007. Data for the present analysis include patients from the January 1, 2007, to December 31, 2007, study period at 280 ACTION hospitals. Participating hospitals are required to submit data to the ACTION registry for all patients who presented within 24 hours of the onset of an ischemic syndrome and if the primary diagnosis was MI (either NSTEMI or STEMI). All participating centers are required to abide by local institutional review or ethical review standards. Baseline characteristics and key outcome data were extracted to a Web-based case record form from existing medical records by a trained data collector at each hospital using standard definitions and did not require direct contact with individual patients. A listing of specific data fields and definitions is available at http://www.ncdr.com/WebNCDR/ACTION/Elements.aspx. Data quality and completeness are monitored by the NCDR Data Quality Program. The NCDR ACTION registry is administered by the American College of Cardiology Foundation and sponsored by Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, Genentech, and Schering-Plough Corporation, who provide material support from the Duke Clinical Research Institute. CKD assessment, covariate definitions, and statistical methods can be found in the online-only Data Supplement. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Study Sample Characteristics

Overall, 19,029 STEMI and 30,462 NSTEMI patients were included in the present analysis; 30.5% and 42.9% of patients with STEMI and NSTEMI, respectively, had CKD of stage 3 or greater (Figure 1). Each stage of CKD was more prevalent in patients with NSTEMI than in those with STEMI, with the exception of stage 3a (Figure 1). With progressively increasing CKD stage, patients were more likely to have hypertension, diabetes mellitus, prior MI, congestive heart failure, and stroke. Additionally, patients with CKD were less likely to be current smokers and had lower body mass index levels (Table 1).

Short-Term Outcomes by CKD Stage

Overall, the risk of mortality increased with CKD stage (Figure 2). Among patients who presented with STEMI, 2.3% of those without CKD died, compared with 8.8%, 17.9%, 27.3%, and 31.8% of those with stage 3a, 3b, 4, and 5 CKD, respectively. In general, a similar trend was observed for NSTEMI, although the absolute event rates were substantially lower. For STEMI, the odds ratios for stage 3a, 3b, 4, and 5 CKD relative to no CKD were 2.5, 3.7, 4.8, and 8.0, respectively ($P_{trend}<0.0001$). For NSTEMI, the odds ratios were 1.8, 2.4, 3.5, and 4.1 ($P_{trend}<0.0001$). However, there was a greater relative increase in death for patients with STEMI with advancing CKD stage than was seen in NSTEMI ($P_{interaction}<0.0001$). In addition, patients with CKD were at higher risk for congestive heart failure than patients with no CKD (Table 2).

Early Therapy and In-Hospital Procedures

Among patients presenting with STEMI, the odds ratio for any reperfusion therapy was significantly lower with worsening CKD stage ($P_{trend}=0.0005$; Table 2) after adjustment for baseline features. However, the use of primary percutaneous coronary intervention ($P_{trend}=0.75$; Table 2) and thrombolytics ($P_{trend}=0.65$) was similar after we accounted for baseline differences. Among those presenting with NSTEMI, patients with CKD were less likely to undergo early invasive therapy ($P_{trend}<0.0001$) or any revascularization ($P_{trend}<0.0001$; Table 2).

Patients presenting with either STEMI or NSTEMI also had higher rates of major bleeding (Table 3) with advancing CKD stage; notably, rates were similar among those with stage 4 and stage 5 CKD. CKD patients presenting with either STEMI or NSTEMI had excess dosing of glycoprotein IIb/IIIa inhibitors ($P_{trend}<0.0001$). For patients presenting with STEMI, those without CKD had a 2.2% rate of glycoprotein IIb/IIIa inhibitor overdosing compared with 55.6% among those with stage 5 CKD ($P_{trend}<0.0001$; Table 3). For patients with NSTEMI, the rate of glycoprotein IIb/IIIa inhibitor overdosing ranged from 2.2% among patients without CKD to 40.9% among patients with stage 5 CKD ($P_{trend}<0.0001$; Table 3).

In-Hospital and Discharge Cardioprotective Medications and Counseling

Rates of early (within 24 hours) in-hospital aspirin use were substantially lower among those with more advanced CKD ($P_{trend}<0.001$ for STEMI and NSTEMI; Figure 3). Similarly, use of clopidogrel, β-blockers, and statins was generally lower among patients with more advanced CKD (all $P_{trend}<0.0001$). In general, similar observations were made for discharge medications. Rates of smoking cessation, dietary and exercise counseling, and referral to cardiac rehabilitation were generally lower for patients with more advanced CKD stage (Figure 3).

Discussion

Principal Findings

Overall, nearly one third of patients presenting with STEMI and >40% of patients presenting with NSTEMI in this
real-world registry had CKD, which is substantially higher than previously recognized in the acute coronary syndrome population. Adjusted rates of adverse outcomes were markedly higher among patients with progressively worse CKD, with odds ratios for death being 4 to 8 times higher among those with stage 5 CKD than among patients without CKD. The present study also documented lower use of short-term therapies, in-hospital procedures, cardioprotective medications, and higher rates of medication overdosing among patients with CKD. Finally, despite these high rates of adverse outcomes, patients with CKD were less likely to receive discharge counseling related to cardiovascular disease risk reduction.

### In the Context of the Current Literature

Patients with CKD, and particularly those undergoing dialysis, are known to have poor outcomes after MI. Using the United States Renal Data System database from 1977 to 1995, patients on dialysis therapy had an overall mortality rate of nearly 90% at 5 years; among patients with MI, almost half experience a cardiac-related death within 2 years. Even with the use of more contemporary data (1998–2000), patients on dialysis presenting with a MI were far more likely to die compared with patients with MI not on dialysis. In addition, the use of coronary interventions and cardioprotective medications among patients with CKD or on dialysis has been shown to be suboptimal.

Previous work from the Global Registry of Acute Coronary Events demonstrated that nearly one third of patients presenting with STEMI or NSTEMI had CKD. Renal subgroup analyses of clinical trials have demonstrated CKD prevalence of 15% to 25% and association with an increased risk of death, albeit not as strong as observed in the present study. Data from the CRUSADE registry initially suggested that nearly 15% of the NSTEMI population had renal dysfunction as defined dichotomously as serum creatinine >2.0 mg/dL (actual serum creatinine values were not available); our findings suggest that nearly 40% of those presenting with NSTEMI have CKD. More contemporary data using the Modification of Diet in Renal Disease equation is more consistent with the findings in the present article.

Our data allowed for comparison of the relationship between CKD and outcomes among patients with both types of MI (NSTEMI and STEMI) collected simultaneously at a single set of hospitals. Although outcomes were poor in patients with CKD with both types of MI, 1 of the more novel findings in the present study was the observation that progressive CKD stage was associated with a steeper gradient of mortality among those presenting with STEMI and CKD compared with NSTEMI and CKD.
The findings from the present study extend the current literature in several important ways. First, these data are derived with the use of a large, nationally representative, real-world registry that included patients from a large number of medical institutions. In addition, several prior studies of outcomes associated with CKD for patients with STEMI and NSTEMI were generated from clinical trials, which tend to exclude patients with advanced renal disease and to encourage specific care
patterns. As such, clinical trial data likely underestimate the true burden and severity of CKD in the MI population and may not provide an accurate assessment of procedure and medication utilization. Second, the present data include not only dialysis patients but also individuals with stage 3 and 4 CKD, the groups that comprise the largest burden of CKD in the United States.31 This allowed for a more comprehensive assessment of CKD in the post-MI population. Third, the present study used data derived from 2007, allowing for an understanding of the contemporary experience of patients with CKD. This is particularly

Table 2. Crude Rates and Adjusted Odds Ratios for In-Hospital Outcomes and In-Hospital Procedures by CKD Stage*

<table>
<thead>
<tr>
<th></th>
<th>No CKD†</th>
<th>Stage 3a CKD</th>
<th>Stage 3b CKD</th>
<th>Stage 4 CKD</th>
<th>Stage 5 CKD or Dialysis</th>
<th>P_trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI CHF, % (n)</td>
<td>4.2 (516)</td>
<td>9.1 (286)</td>
<td>13.6 (195)</td>
<td>19.1 (98)</td>
<td>14.6 (34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>1.7 (1.4–2.1)</td>
<td>2.3 (1.9–2.7)</td>
<td>3.1 (2.4–4.1)</td>
<td>2.8 (2.0–3.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>1.5 (1.2–1.8)</td>
<td>1.6 (1.3–1.9)</td>
<td>1.8 (1.3–2.4)</td>
<td>1.5 (1.1–2.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Primary PCI (STEMI), % (n)</td>
<td>87.1 (9586)</td>
<td>84.6 (2283)</td>
<td>81.4 (857)</td>
<td>75.4 (230)</td>
<td>71.3 (102)</td>
<td>0.84</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>1.1 (0.9–1.3)</td>
<td>1.1 (0.9–1.4)</td>
<td>0.8 (0.6–1.1)</td>
<td>1.0 (0.6–1.8)</td>
<td>0.81</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>1.1 (0.9–1.3)</td>
<td>1.1 (0.9–1.4)</td>
<td>0.8 (0.6–1.2)</td>
<td>1.0 (0.6–1.8)</td>
<td>0.75</td>
</tr>
<tr>
<td>Any reperfusion§, % (n)</td>
<td>95.2 (10 484)</td>
<td>92.5 (2495)</td>
<td>88.9 (936)</td>
<td>83.6 (255)</td>
<td>78.3 (112)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>0.8 (0.7–1.0)</td>
<td>0.7 (0.6–0.8)</td>
<td>0.5 (0.4–0.6)</td>
<td>0.4 (0.3–0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>0.9 (0.8–1.1)</td>
<td>0.9 (0.7–1.1)</td>
<td>0.6 (0.5–0.8)</td>
<td>0.6 (0.4–0.9)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No CKD†</th>
<th>Stage 3a CKD</th>
<th>Stage 3b CKD</th>
<th>Stage 4 CKD</th>
<th>Stage 5 CKD or Dialysis</th>
<th>P_trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSTEMI CHF, % (n)</td>
<td>4.4 (691)</td>
<td>8.3 (454)</td>
<td>12.6 (470)</td>
<td>17.3 (296)</td>
<td>11.6 (118)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>1.6 (1.4–1.8)</td>
<td>2.1 (1.8–2.5)</td>
<td>2.9 (2.4–3.5)</td>
<td>2.2 (1.8–2.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>1.3 (1.2–1.5)</td>
<td>1.5 (1.3–1.7)</td>
<td>1.9 (1.6–2.3)</td>
<td>1.3 (1.1–1.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Early invasive (NSTEMI), % (n)</td>
<td>77.8 (12 516)</td>
<td>67.7 (3433)</td>
<td>54.7 (1614)</td>
<td>36.7 (383)</td>
<td>48.9 (372)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>0.8 (0.7–0.9)</td>
<td>0.5 (0.5–0.6)</td>
<td>0.3 (0.2–0.3)</td>
<td>0.4 (0.3–0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>0.9 (0.8–1.0)</td>
<td>0.7 (0.6–0.8)</td>
<td>0.4 (0.3–0.5)</td>
<td>0.6 (0.5–0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any revascularization§, % (n)</td>
<td>71.8 (10 491)</td>
<td>62.0 (2868)</td>
<td>50.8 (1356)</td>
<td>41.2 (387)</td>
<td>48.9 (334)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>0.8 (0.8–0.9)</td>
<td>0.6 (0.5–0.6)</td>
<td>0.5 (0.4–0.5)</td>
<td>0.5 (0.4–0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)‡</td>
<td>1.0 (reference)</td>
<td>0.9 (0.9–1.0)</td>
<td>0.7 (0.7–0.8)</td>
<td>0.6 (0.5–0.7)</td>
<td>0.8 (0.7–1.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; n, number of events; OR, odds ratio; CI, confidence interval; and PCI, percutaneous coronary intervention.

*Denominators may vary on the basis of the individual exclusions for different outcomes.
†The “no CKD” category is limited by the lack of albuminuria.
‡Multivariable models adjusted for age, sex, body mass index, race, insurance status, hypertension, diabetes mellitus, recent/current smoker, hypercholesterolemia, prior peripheral arterial disease, prior MI, prior percutaneous coronary intervention, prior coronary artery bypass graft surgery, history of heart failure, history of stroke, signs of heart failure, admission heart rate, and systolic blood pressure.
§Any reperfusion defined as use of primary percutaneous coronary intervention or fibrinolytic medications.
‖Any revascularization defined as percutaneous coronary intervention or coronary artery bypass grafting.
important in the context that in 2002, several key articles described the increased mortality of patients with CKD in the acute MI setting and the relative underutilization of known cardioprotective therapies compared with patients without CKD.\(^{21-24}\) Thus, several years later, limited progress has been made.

**Potential Mechanisms for Worse Clinical Outcomes**

Patients with CKD have higher rates of preexisting cardiovascular disease and more severe cardiovascular disease on presentation with acute coronary syndrome, which in part may contribute to their poorer outcomes. In addition, the findings from the present study, as well as work from prior studies, indicate underutilization of known cardioprotective therapies in patients with CKD and more frequent errors in dosing when used, which may further contribute to the poor outcomes observed in this group. Indeed, many therapies have not been studied specifically in CKD and in patients on dialysis because nephrology patients are the least likely of all internal medicine subspecialty patients to be studied in clinical trials.\(^{25,26}\)

Furthermore, some data suggest that known interventions and proven therapies in the general population may not provide benefits to end-stage renal disease patients. For example, the 4-D Trial, which enrolled patients with diabetes mellitus and end-stage renal disease on dialysis, demonstrated increased risk of fatal stroke among those randomized to statin therapy versus placebo.\(^{32}\) Therefore, the avoidance of certain cardioprotective medications in dialysis patients may be driven in part by the lack of clinical trial data to support their efficacy rather than by errors of omission. The reduced utilization of invasive procedures, particularly in NSTEMI patients, in whom the decision making is less protocol or critical pathway driven than in STEMI patients, may also reflect a desire to balance cardioprotective effects of procedures with the desire to avoid further damaging kidney function. This may be reflected by the lowest relative utilization of cardiac catheterization, percutaneous coronary intervention, or coronary artery bypass graft surgery, history of heart failure, history of stroke, signs of heart failure, admission heart rate, and systolic blood pressure.

---

**Table 3. Crude Rates and Adjusted Odds Ratios for In-Hospital Adverse Outcomes by CKD Stage***

<table>
<thead>
<tr>
<th>Stage 5 CKD or Dialysis</th>
<th>No CKD†</th>
<th>Stage 3a CKD</th>
<th>Stage 3b CKD</th>
<th>Stage 4 CKD</th>
<th>(P_{trend})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-CABG major bleed, % (n)</td>
<td>8.8 (999)</td>
<td>14.7 (420)</td>
<td>23.1 (304)</td>
<td>26.6 (128)</td>
<td>26.4 (58)</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>1.5 (1.3–1.7)</td>
<td>2.4 (2.0–2.8)</td>
<td>2.7 (2.2–3.3)</td>
<td>2.6 (2.0–3.9)</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)†</td>
<td>1.0 (reference)</td>
<td>1.4 (1.2–1.6)</td>
<td>2.0 (1.7–2.4)</td>
<td>2.0 (1.6–2.5)</td>
<td>2.1 (1.4–2.9)</td>
</tr>
<tr>
<td>GPIb/IIa excess dosing</td>
<td>2.2 (114)</td>
<td>19.1 (250)</td>
<td>49.2 (216)</td>
<td>57.0 (57)</td>
<td>55.6 (10)</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>5.1 (4.0–6.5)</td>
<td>21.3 (14.5–31.3)</td>
<td>25.9 (12.1–55.7)</td>
<td>39.1 (14.1–108.2)</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)†</td>
<td>1.0 (reference)</td>
<td>6.4 (4.9–8.2)</td>
<td>38.0 (22.0–65.9)</td>
<td>42.7 (16.3–112.2)</td>
<td>51.0 (16.0–162.6)</td>
</tr>
<tr>
<td>Antithrombin excess dosing‡</td>
<td>72.3 (832)</td>
<td>74.9 (206)</td>
<td>72.2 (70)</td>
<td>80.8 (21)</td>
<td>37.5 (3)</td>
</tr>
<tr>
<td>Age-, race-, sex-adjusted OR (95% CI)</td>
<td>1.0 (reference)</td>
<td>1.2 (0.9–1.6)</td>
<td>1.2 (0.7–1.8)</td>
<td>1.8 (0.6–5.4)</td>
<td>0.3 (0.1–0.7)</td>
</tr>
<tr>
<td>Multivariable-adjusted OR (95% CI)†</td>
<td>1.0 (reference)</td>
<td>1.2 (0.9–1.7)</td>
<td>1.2 (0.7–1.8)</td>
<td>1.9 (0.6–6.3)</td>
<td>0.3 (0.1–0.7)</td>
</tr>
</tbody>
</table>

---

*Denominators may vary on the basis of the individual exclusions for different outcomes.
†Multivariable models adjusted for age, sex, body mass index, race, insurance status, hypertension, diabetes mellitus, recent/current smoker, hypercholesterolemia, prior peripheral arterial disease, prior MI, prior percutaneous coronary intervention, prior coronary bypass graft surgery, history of heart failure, history of stroke, signs of heart failure, admission heart rate, and systolic blood pressure.
‡Includes dosing above guideline recommendations for unfractionated heparin with fibrinolytics in STEMI and for unfractionated heparin or low–molecular-weight heparin in NSTEMI.
§Includes dosing above guideline recommendations for antithrombin excess dosing.
Figure 3. Crude rates of acute in-hospital medications (within 24 hours), discharge medications, and discharge counseling by CKD status. All $P_{\text{trend}}<0.001$ across CKD stages except for aspirin as a discharge medication and referral to cardiac rehabilitation (STEMI; $P_{\text{trend}}=0.02$ for both) and β-blockers as a discharge medication ($P_{\text{trend}}=0.50$ [STEMI], $P_{\text{trend}}=0.12$ [NSTEMI]). The “no CKD” category is limited by lack of information on albuminuria.
Although the use of invasive procedures may be limited in part by a desire to avoid worsening kidney function, and the use of medications may be limited by lack of evidence or concerns for complications, no clear barriers should exist for low-risk interventions such as discharge counseling. We observed a lower rate of counseling for lifestyle modification by CKD stage among those considered to have no contraindication for an intervention.

**Strengths and Limitations**

The major strength of the present study includes the use of a nationally representative registry, providing real-world data that are more generalizable than results from single-center registries. These data extend previous data using binary cut points or focusing on dialysis patients by demonstrating gradients of risk and therapy utilization by severity of CKD. Additionally, the use of registry data eliminates the selection bias of clinical trials. Furthermore, we had very large numbers of patients with CKD presenting with both STEMI and NSTEMI, enabling a detailed analysis by CKD stage and MI type. We were also able to examine post-MI outcomes and processes at several levels, including in-hospital clinical outcomes, procedure utilization, and cardioprotective medication and counseling use. Certain limitations of the present analysis warrant discussion. Because the data are derived from a hospital-based registry, patients who died before admission to the hospital were by definition excluded from the registry, and therefore mortality may be underestimated. Furthermore, we evaluated only short-term in-hospital outcomes; however, long-term outcomes related to CKD and dialysis post-MI have been described previously. Data were extracted from hospitals with differing creatinine assays and standards, and no standard central determination of kidney function was performed. However, these data reflect actual clinical practice and the information about kidney function that was available to treating physicians when therapeutic decisions were made. There were too few patients with estimated glomerular filtration rate <15 to separately examine those not on dialysis. Finally, we did not have information on albuminuria and proteinuria.

**Implications**

The most striking finding from this study is the high rate of CKD in the MI population. Clinicians should be aware of the high likelihood of concomitant CKD and cardiovascular disease in patients presenting with MI to allow for appropriate treatment decisions and to adjust medication dosing. In addition, these findings underscore the high mortality rates and frequent adverse outcomes associated with CKD in the setting of MI, as well as the need to direct clinical trials aimed specifically at this high-risk subgroup in order to identify optimal therapies and treatment for these patients. The underutilization of evidence-based therapies, procedures, and counseling in the CKD population is an opportunity for quality improvement in the care of high-risk patients.

**Conclusions**

Reports over the past decade have highlighted the importance of CKD among patients with MI. Data from this contemporary cohort suggest that patients with CKD still receive fewer evidence-based therapies and have substantially higher mortality rates. Additional research to define optimal post-MI care in patients with CKD is warranted.

**Sources of Funding**

The ACTION registry is supported by Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, Genentech, and Schering-Plough Corporation.

**Disclosures**

The authors report the following conflicts of interest: Dr Kontos—speakers’ bureau: Sanofi-Aventis, Schering-Plough, Pfizer; consultant: Sanofi-Aventis, Schering-Plough, Pfizer, Inovise Technologies, Molecular Insight Pharmaceuticals; research support: Amersham/GE, Inovise Technologies, Biosite, Molecular Insight Pharmaceuticals. Dr Saucedo—consultant: Eli Lilly, Bristol-Myers Squibb/Sanofi, The Medicines Company; research, honoraria: Schering-Plough; honoraria: Pfizer, Dr Wiviott—consultant: Sanofi-Aventis; research, honoraria: Eli Lilly; research, honoraria: Daichi Sankyo; honoraria: Astra-Zeneca; research: Schering-Plough; honoraria: Pfizer. Dr Roe—research funding and consultant and member of the speakers’ bureau for the companies that fund the ACTION registry via the American College of Cardiology: BMS/Sanofi-Aventis, Schering-Plough. Dr Cannon—research grants/support from the following companies: Accumetrics, AstraZeneca, Bristol-Myers Squibb/Sanofi Partnership, GlaxoSmithKline, Merck, Merck/Schering-Plough Partnership; clinical advisor, equity in Automedics Medical Systems. The other authors report no conflicts.

**References**

12. Ferrer-Hita JJ, Dominguez-Rodriguez A, Garcia-Gonzalez MJ, Breu-Gonzalez P. Renal dysfunction is an independent predictor of in-hospital...
Chronic kidney disease (CKD) is a risk factor for myocardial infarction (MI) and death. We sought to characterize the association between CKD severity and short-term outcomes and the use of in-hospital evidence-based therapies among patients with ST-segment elevation MI (STEMI) and non–ST-segment elevation MI (NSTEMI) using the Acute Coronary Treatment and Intervention Outcomes Network registry, a nationwide sample of STEMI and NSTEMI patients admitted to hospitals in the United States. Overall, 30.5% and 42.9% of patients with STEMI and NSTEMI, respectively, had CKD. Regardless of MI type, patients with progressively more severe CKD had higher rates of death. In addition, patients with progressively more severe CKD were less likely to receive immediate evidence-based therapies including aspirin, β-blockers, or clopidogrel, were less likely to undergo any reperfusion (STEMI) or revascularization (NSTEMI), and had higher rates of bleeding. We conclude that a large proportion of patients presenting with STEMI or NSTEMI have CKD and have increased in-hospital mortality rates. These patients receive fewer evidence-based therapies. Additional research is needed to define optimal post-MI care in patients with CKD is warranted.
Use of Evidence-Based Therapies in Short-Term Outcomes of ST-Segment Elevation Myocardial Infarction and Non–ST-Segment Elevation Myocardial Infarction in Patients With Chronic Kidney Disease: A Report From the National Cardiovascular Data Acute Coronary Treatment and Intervention Outcomes Network Registry

Caroline S. Fox, Paul Muntner, Anita Y. Chen, Karen P. Alexander, Matthew T. Roe, Christopher P. Cannon, Jorge F. Saucedo, Michael C. Kontos and Stephen D. Wiviott

_Circulation_. 2010;121:357-365; originally published online January 11, 2010;
doi: 10.1161/CIRCULATIONAHA.109.865352

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/121/3/357

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2010/01/12/CIRCULATIONAHA.109.865352.DC1

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

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

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/
SUPPLEMENTAL MATERIAL

Use of Evidence-Based Therapies in and Short-term Outcomes of STEMI and NSTEMI in Patients with Chronic Kidney Disease: A Report from the National Cardiovascular Data ACTION Registry

Fox CS et al.

Methods Supplement

Study Sample

Patients for this study were drawn from the National Cardiovascular Data Registry (NCDR) Acute Coronary Treatment and Intervention Outcomes Network (ACTION) registry, a nationally-representative, quality improvement registry of ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI) that began enrolling patients January 1, 2007. Data for the present analysis includes patients from the January 1, 2007 to December 31, 2007 study period at 280 ACTION Hospitals. Participating hospitals are required to submit data to the ACTION registry for all patients who presented within 24 hours of the onset of an ischemic syndrome, and if the primary diagnosis was myocardial infarction (either NSTEMI or STEMI). All participating centers are required to abide by local institutional review or ethical review standards. Baseline characteristics and key outcome data were extracted to a web-based case record form from existing medical records using a trained data collector at each hospital using standard definitions, and did not require direct contact with individual patients. A listing of specific data fields and definitions is available at http://www.ncdr.com/WebNCDR/ACTION/Elements.aspx. For this analysis, patients were excluded if data was missing for serum creatinine status (n=452 for STEMI patients; n=574 for NSTEMI patients). Data quality and completeness is monitored by the
NCDR Data Quality Program. The NCDR ACTION Registry is administered by the American College of Cardiology Foundation (ACCF) and sponsored by Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, Genentech, and Schering-Plough Corporation who provide material support for the operation of the data collection and infrastructure. The sponsors had no additional role in this project including the selection of topic, analysis of data, decision to publish, or approval of the manuscript prior to publication. Data analysis was performed by a statistician independent of the sponsors (AYC) from the Duke Clinical Research Institute. The authors had access to the data and take full responsibility for its integrity.

Assessment of Chronic Kidney Disease (CKD)

CKD was assessed based on serum creatinine measurements, and chronic dialysis was determined based on physician report and local medical record review. Serum creatinine was transformed to estimated glomerular filtration rate (eGFR) via the MDRD equation (eGFR = 186*(Serum Creatinine)^-1.154 * age^-0.203 * (0.742 if female) * (1.21 if African-American). CKD was analyzed by stages: Stage 3a CKD was defined as an eGFR between 45 and 59 ml/min/1.73m^2; Stage 3b as eGFR 30-44 ml/min/1.73m^2; Stage 4 CKD as eGFR between 15 and 29 ml/min/1.73m^2, and Stage 5 CKD as an eGFR < 15 ml/min/1.73m^2 or dialysis therapy (hereafter referred to as Stage 5 CKD).

Outcome variables

The primary outcome of interest was short-term in-hospital death. We also examined in-hospital congestive heart failure and major bleeding. Major bleeding was defined as an absolute hematocrit drop of ≥12%, an intracranial hemorrhage, a retroperitoneal hemorrhage, or transfusion (either with baseline hematocrit ≥28%, or baseline hematocrit<28% and a witnessed bleeding event). Patients were excluded if they were transferred out of an ACTION hospital as
clinical outcome assessment was incomplete. All outcomes were ascertained from the ACTION data collection form based on medical record abstraction at each participating hospital using standard definitions. Excess dosing with antithrombin agents or glycoprotein IIb/IIIa receptor antagonists was derived from medication dosing based on previous work. In addition, excess dosing of antithrombin agents, also derived from previous work, include the initial use of unfractionated heparin (UFH) and/or low molecular weight heparin (LMWH; antithrombins) for NSTEMI patients, and the initial use of UFH with thrombolytics only for STEMI patients.

We also explored the use of in-hospital acute reperfusion in STEMI including fibrinolysis or primary percutaneous coronary intervention (PCI) or an early invasive strategy in NSTEMI (cardiac catheterization within 48 hours of presentation) or CABG. We evaluated the use of known cardio-protective medications (aspirin, clopidogrel, beta-blocker, statin treatment) both acutely in-hospital (within 24 hours of presentation) and upon discharge. Finally, we assessed the rates of guideline recommended discharge counseling, including smoking cessation, diet, and exercise and referral for cardiac rehabilitation. For all analyses, the denominator consisted of eligible patients without contraindication based on the specific outcome of interest.

**Statistical Methods**

Patient baseline characteristics, use of treatments and interventions, and in-hospital clinical outcomes were summarized by CKD stage for individuals presenting with STEMI or NSTEMI, separately. Continuous and ordinal categorical variables were compared using stratum-adjusted Kruskal Wallis tests (in which stratification was by hospital), while nominal categorical variables were compared using the Cochran-Armitage test.

To explore associations of CKD stages (compared with no CKD) and use of guidelines-recommended treatments, interventions, and in-hospital outcomes, logistic generalized
estimating equations method with exchangeable working correlation matrix was used to account for within-hospital clustering, where patients at the same hospital were more likely to have similar responses relative to patients in other hospitals (i.e. within-center correlation for responses). Two models were performed: 1) minimally-adjusted model, including age, gender, race; 2) multivariable model including age, gender, race, body mass index (BMI), insurance status, hypertension, diabetes, recent/current smoker, hypercholesterolemia, prior peripheral arterial disease (PAD), prior myocardial infarction (MI), prior percutaneous coronary intervention, prior coronary bypass graft surgery, history of heart failure, history of stroke, signs of heart failure, admission heart rate and systolic blood pressure. P-values for the trends across CKD stage were obtained by modeling CKD stage as an ordinal independent variable.

Adjusted associations are displayed as odds ratios (OR) (95% confidence interval [CI]). A $P$ value <0.05 was considered significant for all tests. All analyses were performed using SAS software (version 9.1, SAS Institute, Cary, North Carolina).

Reference List
