Longitudinal Risk of Adverse Events in Patients With Acute Kidney Injury After Percutaneous Coronary Intervention

Insights From the National Cardiovascular Data Registry

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Background—Acute kidney injury (AKI) remains a common complication after percutaneous coronary intervention (PCI) and is associated with adverse in-hospital patient outcomes. The incidence of adverse events after hospital discharge in patients having post-PCI AKI is poorly defined, and the relationship between AKI and outcomes after hospital discharge remains understudied.

Methods and Results—Using the National Cardiovascular Data Registry CathPCI registry, we assessed the incidence of AKI among Medicare beneficiaries after PCI from 2004 to 2009 and subsequent post-discharge adverse events at 1 year. AKI was defined using Acute Kidney Injury Network (AKIN) criteria. Adverse events included death, myocardial infarction, bleeding, and recurrent kidney injury. Using Cox methods, we determined the relationship between in-hospital AKI and risk of post-discharge adverse events by AKIN stage. In a cohort of 453 475 elderly patients undergoing PCI, 39 850 developed AKI (8.8% overall; AKIN stage 1, 85.8%; AKIN 2/3, 14.2%). Compared with no AKI, in-hospital AKI was associated with higher post-discharge hazard of death, myocardial infarction, or bleeding (AKIN 1: hazard ratio [HR], 1.53; confidence interval [CI], 1.49–1.56 and AKIN 2/3: HR, 2.13; CI, 2.01–2.26), recurrent AKI (AKIN 1: HR, 1.70; CI, 1.64–1.76; AKIN 2/3: HR, 2.22; CI, 2.04–2.41), and AKI requiring dialysis (AKIN 1: HR, 2.59; CI, 2.29–2.92; AKIN 2/3: HR, 4.73; CI, 3.73–5.99). For each outcome, the highest incidence was within 30 days.

Conclusions—Post-PCI AKI is associated with increased risk of death, myocardial infarction, bleeding, and recurrent renal injury after discharge. Post-PCI AKI should be recognized as a significant risk factor not only for in-hospital adverse events but also after hospital discharge. **(*Circ Cardiovasc Interv*. 2017;10:e004439. DOI: 10.1161/CIRCINTERVENTIONS.116.004439.)**

Key Words: morbidity ■ mortality ■ outcome assessment (health care) ■ percutaneous coronary intervention ■ renal insufficiency

Acute kidney injury (AKI) is a common complication after percutaneous coronary intervention (PCI)[1,2] and is associated with significant morbidity and mortality. Most studies evaluating the development of post-PCI AKI and its association with adverse outcomes of bleeding, myocardial infarction (MI), and death have focused on in-hospital adverse events, with relatively few focusing on longitudinal, post-discharge outcomes.[1–13] Furthermore, a majority of studies defining these relationships have occurred in single centers and small cohorts, preceding widespread use of guideline-recommended strategies for prevention of AKI,[14–16] using varying definitions of AKI, and without investigation of the longitudinal relationship between post-PCI AKI and recurrent renal injury. Finally, a broader understanding of when these events occur during follow-up is lacking, missing an opportunity to define the highest periods of risk for post-PCI AKI patients.

A recent analysis from the National Cardiovascular Data Registry (NCDR) using the Acute Kidney Injury Network (AKIN) definition of AKI[17] evaluated the incidence, predictors, and in-hospital outcomes of post-PCI patients having

Received August 25, 2016; accepted March 6, 2017.

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The Data Supplement is available at http://circinterventions.ahajournals.org/lookup/suppl/doi:10.1161/CIRCINTERVENTIONS.116.004439/-/DC1.

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WHAT IS KNOWN

- Acute kidney injury remains a common complication after percutaneous coronary intervention.
- Development of acute kidney injury after percutaneous coronary intervention is associated with adverse in-hospital patient outcomes, but its relationship with longitudinal, post-discharge events has been understudied.

WHAT THIS STUDY ADDS

- Development of acute kidney injury is associated with increased rates of death, myocardial infarction, bleeding, and recurrent renal injury after discharge, with the hazard of adverse events increasing with the severity of the acute kidney injury.
- These events occur most frequently in the first 30 days, but increased rates for adverse events persist to 1 year after hospital discharge.
- Acute kidney injury after percutaneous coronary intervention should be recognized as a risk factor for adverse events after hospital discharge, especially in the first 30 days.

AKI.[1] This study represents the largest evaluation of AKI in a contemporary PCI cohort to date and used a standardized definition of AKI that has been adopted by nephrology, critical care, and cardiology communities alike.[4,6,17,18] However, the association between post-PCI AKI and adverse events after hospital discharge remain less well defined, with the risk of recurrent renal injury understudied and the timing of these events unknown. Understanding this relationship in the context of contemporary PCI care may help distinguish those patients who remain at risk for adverse events after discharge and may identify a period of vulnerability where risk is greatest.

Accordingly, we used the NCDR CathPCI registry to evaluate the relationship between post-PCI AKI and the incidence of adverse events after hospital discharge. By leveraging one of the world's largest PCI registries, we sought to better define the associations of post-PCI AKI and adverse events in a contemporary setting, with standard and accepted definitions of the AKI exposure. Understanding this relationship and the timing of these events in a large, multicenter, real-world population may aid clinicians in the identification of critical periods of vulnerability for patients after PCI.

Methods

Study Population

The NCDR CathPCI Registry has been described previously.[19,20] The registry collects data on all patients undergoing PCI at >1400 institutions within the United States. These data elements were prospectively defined by a committee of the American College of Cardiology and are available on the NCDR website, including patient and hospital characteristics, clinical presentation, treatments, and outcomes associated with PCI. These data are entered at each participating institution using an American College of Cardiology–certified interface and are exported to a central repository in a standard format. The data undergo annual evaluation by the Data Quality Program, with audits of >50 rotating data fields across randomly selected participating institutions.[20,21] For this study, the CathPCI registry was linked to Center for Medicare & Medicaid Services (CMS) billing data, to allow for a longitudinal analysis of elderly patients undergoing PCI and their outcomes after hospital discharge.[22,23]

For this analysis, we identified all patients undergoing PCI at institutions with linked CMS data between November 29, 2004, and December 31, 2009 (n=877 029 patients at 1127 sites). To accurately define in-hospital AKI, we excluded patients who did not have both a pre-procedure and peak postprocedure in-hospital serum creatinine level (missing both n=251 828 [28.7%]; missing pre-procedure n=16 830 [1.9%]; missing postprocedure n=96 415; [11.0%]), as well as patients who were on dialysis at the time of PCI (n=10 296; 1.17%). To ensure the capture of longitudinal post-discharge events, we excluded patients not eligible for Medicare Fee-for-Service (n=26 969; 3.08%). The final cohort included 453 475 patients undergoing PCI during the study period.

Primary Exposure

The primary exposure was development of AKI, using AKIN criteria to define both an episode of AKI and the severity of the injury. AKIN criteria defines 3 stages of kidney injury with AKIN stage 1 classified as a ≥0.3 mg/dL absolute or 1.5- to 2.0-fold increase in serum creatinine from baseline, AKIN stage 2 as a >2- to 3-fold increase in serum creatinine, and AKIN stage 3 as a serum creatinine >4.0 mg/dL with an acute increase of ≥0.5 mg/dL or a >3-fold increase in serum creatinine.[17] Development of AKI was divided into no AKI, AKIN stage I, or AKIN stage 2 or 3. AKIN stages 2 and 3 were a priori combined, to ensure adequate cohort size for statistical analysis. AKIN stage was determined using pre-procedure serum creatinine and peak postprocedure serum creatinine.

Outcomes

The primary outcome of interest was a composite of death, MI, and bleeding-related hospitalization within 1 year of hospital discharge from the index PCI. Secondary end points were post-discharge hospitalizations for AKI or AKI requiring dialysis, as well as individual events of death, MI, or bleeding-related hospitalization. Deaths were determined using data from CMS vital status files. Bleeding-related hospitalizations, MI, and AKI-related hospitalizations were determined using administrative data, utilizing billing codes submitted to CMS from *The International Classification of Disease*, Ninth Revision, Clinical Diagnosis Code for events after discharge from the initial PCI encounter (Table I in the Data Supplement). Episodes of AKI requiring dialysis were determined using *The International Classification of Disease*, Ninth Revision, Clinical Diagnosis Code procedure codes for hemodialysis in addition to a hospital diagnosis of AKI.

Statistical Analysis

Patients were stratified by the presence and severity of in-hospital AKI by AKIN criteria: no AKI, AKIN stage 1, and AKIN stage 2 or 3. AKIN stages 2 and 3 were a priori combined into 1 stratum out of concerns that AKIN stage 3 would have too few patients for independent modeling in the primary analysis. Differences between groups were compared using χ^2 or Fisher exact tests for categorical variables and Wilcoxon rank-sum and Kruskal–Wallis tests for continuous variables.

The cumulative incidence of the primary and secondary end points was determined, stratified by in-hospital AKI status. To assess the association between development of in-hospital AKI with the primary and secondary outcomes, we used Cox proportional hazards models for each outcome. Patients were censored for either the end of their Fee-for-Service eligibility or the end of the observation period (December 31, 2009). A robust sandwich variance estimator was used to account for clustering of events within hospitals. Covariates for adjustment were chosen from the NCDR PCI mortality model.[24] These included sex, age, race, body mass index, history of cerebrovascular disease, peripheral artery disease,

congestive heart failure, diabetes mellitus, chronic lung disease, previous valve surgery, previous PCI, ejection fraction, New York Heart Association functional class, glomerular filtration rate, a coronary lesion of >50%, presence of cardiogenic shock on presentation, symptom status on presentation, PCI status (elective, urgent, emergent, or salvage), insertion of an intra-aortic balloon pump, and preprocedural TIMI (Thrombolysis in Myocardial Infarction) coronary blood flow.

Secondary Analyses

We performed a secondary analysis evaluating patients by each individual stage of AKIN kidney injury, analyzing AKIN stages 1, 2, and 3 independently. We determined the relationship between presence and severity of in-hospital AKI by each of the 4 possible categories of post-PCI in-hospital AKI (no AKI, AKIN stage 1, AKIN stage 2, and AKIN stage 3) for the primary and secondary end points. Cox proportional hazards with similar adjustment were calculated for post-discharge death, MI, and bleeding, as well as rehospitalization for AKI, and AKI requiring dialysis.

As a large number of patients were missing either a pre- or post-procedure creatinine, we also compared patient-level demographic, clinical, and procedural characteristics of those patients missing peri-procedural assessment of renal function with those included in our cohort. We hypothesized that patients undergoing incomplete peri-procedural assessment of renal function would be more likely to have less comorbidities and lower acuity of presentation for PCI than those included in the primary cohort.

Results

Baseline Characteristics

Of the 453 475 patients in the study cohort, 39 850 developed in-hospital AKI after PCI (8.8%). These represented 34 207 cases of AKIN stage 1 (7.5%) and 5643 cases of AKIN stage 2 or 3 (1.2%) severity. The mean age in the cohort was 75.1 years (±SD 6.74), with 42.1% (n=191 104) women (Table 1). There was a high prevalence of comorbidities, with 34.1% of the population having a history of diabetes mellitus (n=154 482), 26.4% with previous MI (n=119 561), and 30.1% with previous PCI (n=136 490). The majority of patients presented with acute coronary syndrome (66.95%; n=303 610), and over half had multivessel coronary artery disease on diagnostic angiography (57.2%; n=259 472). Mean contrast volume was 208.1 mL (SD, 99.4). Mean ejection fraction was 51.5% (SD, 13.5). Nearly half of the cohort had evidence of at least moderate renal insufficiency at presentation (42.6% with glomerular filtration rate, <60 mL/min per 1.73 m^2; n=193 177; mean glomerular filtration rate, 63.99). Baseline median serum creatinine was 1.2 mg/dL (SD, 0.5).

Clinical characteristics associated with the development of in-hospital AKI included a history of diabetes mellitus,

Table 1. Demographics, Clinical History, and Baseline Clinical Characteristics

Demographics	Overall (n=453 475)	No AKI (n=413 625)	AKIN 1 (n=34 207)	AKIN 2/3 (n=5643)	*P* Value
Age, mean±SD, y	75.1±6.7	74.9±6.7	76.8±7.1	76.7±7.1	<0.0001
Male sex, %	57.9	58.4	53.3	48.3	<0.0001
Body mass index, mean±SD, kg/m^2	28.5±5.8	28.4±5.8	28.8±6.4	29.2±6.9	<0.0001
Previous myocardial infarction, %	26.4	26.1	29.1	27.5	<0.0001
Congestive heart failure, %	14.6	13.5	24.9	26.4	<0.0001
Diabetes mellitus, %	34.1	33.0	44.2	47.9	<0.0001
Prevous AKI, %	5.6	4.8	13.6	13.4	<0.0001
Cerebrovascular disease, %	16.7	16.1	22.1	22.6	<0.0001
Peripheral vascular disease, %	15.6	15.0	21.0	21.6	<0.0001
Chronic lung disease, %	19.6	19.1	24.6	25.8	<0.0001
Hypertension, %	82.9	82.6	85.9	84.6	<0.0001
Tobacco history, %					0.03
Never	41.3	41.3	41.6	41.8	
Former	37.0	37.1	36.3	36.1	
Current	11.4	11.4	10.9	11.1	
Dyslipidemia, %	75.8	76.1	72.2	70.4	<0.0001
Family history of early CAD, %	18.6	18.9	15.7	14.8	<0.0001
Previous PCI, %	30.1	30.5	26.6	23.1	<0.0001
Previous CABG, %	23.0	23.0	23.9	22.3	<0.0001
Ejection fraction, mean±SD, %	51.5±13.5	52.1±13.2	46.0±15.3	43.5±15.9	<0.0001
Glomerular filtration rate, mean±SD, mL/min per 1.73 m^2	65.7±26.2	66.0±21.5	59.1±27.4	81.5±127.3	<0.0001
Serum creatinine, mean±SD, mg/dL	1.2±0.5	1.2±0.5	1.4±0.7	1.2±0.5	<0.0001

AKI indicates acute kidney injury; AKIN, Acute Kidney Injury Network stage; CABG, coronary artery bypass grafting; CAD, coronary artery disease; and PCI, percutaneous coronary intervention.

Table 2. Clinical Presentation for PCI and Procedural Details

	Overall	No AKI	AKIN 1	AKIN 2/3	*P* Value
Clinical presentation					
Heart failure, %	14.1	12.5	29.4	36.3	<0.0001
NYHA class, %					<0.0001
Class 1	25.2	25.9	18.3	15.8	
Class 2	21.7	22.4	15.7	12.7	
Class 3	29.7	29.7	30.2	27.3	
Class 4	22.0	20.6	34.7	43.1	
Cardiogenic shock, %	2.7	2.1	8.3	17.3	<0.0001
PCI presentation					<0.0001
No angina/symptoms	12.7	12.9	10.9	9.9	
Atypical chest pain	6.2	6.4	4.3	3.1	
Stable angina	14.1	14.8	7.6	4.8	
Unstable angina	33.3	34.1	26.0	20.1	
Non-STEMI	20.0	19.1	29.3	31.4	
STEMI	13.6	12.7	22.0	30.8	
PCI status					<0.0001
Elective	44.0	45.6	28.4	21.4	
Urgent	40.7	40.3	45.3	40.4	
Emergent	15.1	13.9	25.3	35.9	
Salvage	0.3	0.2	1.1	2.3	
PCI details					
Contrast volume, mL; mean±SD	208.1±99.4	206.9±98.2	216.8±108.0	238.4±119.1	<0.0001
Access site					<0.0001
Femoral	97.9	97.9	97.6	97.8	
Brachial	0.4	0.4	0.6	0.6	
Radial	1.3	1.3	1.3	1.0	
Intra-aortic balloon pump, %	3.0	2.2	9.8	20.8	<0.0001
No. of diseased vessels, %					<0.0001
1	38.8	39.7	30.7	27.2	
2	31.1	31.0	32.2	32.9	
3	26.1	25.3	33.7	37.1	
Multivessel PCI, %	15.2	15.0	17.1	18.0	<0.0001
Stent type, %					<0.0001
Drug eluting	67.9	68.8	58.8	54.0	
Bare metal	24.7	24.2	30.4	32.0	
No stent used	7.4	7.0	10.8	14.0	
Pre-PCI stenosis, %					<0.0001
<50	0.1	0.1	0.1	0.2	
50–69	0.9	0.9	0.6	0.8	
70–99	84.4	85.3	76.0	67.5	
100	14.6	13.7	23.3	31.5	

(*Continued*)

Table 2. Continued

	Overall	No AKI	AKIN 1	AKIN 2/3	*P* Value
Pre-PCI TIMI flow					<0.0001
0	13.9	13.0	22.4	29.8	
1	10.6	10.5	11.3	12.2	
2	20.4	20.4	20.0	18.9	
3	54.4	55.4	45.8	38.7	

AKI indicates acute kidney injury; AKIN, Acute Kidney Injury Network; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and TIMI, Thrombolysis in Myocardial Infarction.

MI, peripheral vascular disease, heart failure, and previous episodes of renal failure (P<0.001 for all; Table 1). In addition, median baseline creatinine clearance and glomerular filtration rate were significantly lower and previous episodes of renal failure were more common among patients developing in-hospital AKI, as compared with those patients who did not develop kidney injury (P<0.001 for all). Finally, median and mean ejection fraction were lower in patients developing in-hospital AKI (P<0.001). Procedural characteristics associated with development of in-hospital AKI included presentation for PCI with ST-segment–elevation MI, non–ST-segment–elevation MI, or cardiogenic shock (Table 2), and the presence of multivessel coronary artery disease on diagnostic angiography. Increased acuity of PCI (urgent and emergent) was more common among those patients developing in-hospital AKI, as was performance of multivessel PCI. Finally, median contrast volumes were also higher in patients developing in-hospital AKI.

Unadjusted Outcomes

The primary outcome of composite death, MI, or bleeding within 1 year of hospital discharge was most frequent in patients having AKIN stage 2 or 3 in-hospital AKI, as compared with patients having AKIN stage 1 in-hospital AKI or no AKI (AKIN 2/3: 34.1% versus AKIN 1: 24.0% versus no AKI: 11.1%; P<0.001). Death at 1 year was most common among patients having AKIN stage 2/3 (AKIN 2/3: 27.9% versus AKIN 1: 17.4% versus no AKI: 6.5%, P<0.001), as was MI (6.6% versus 6.3% versus 3.4%; P<0.001), and rehospitalization for bleeding (3.4% versus 3.0% versus 1.9%; P<0.001). Rehospitalization for AKI was most common among patients having AKIN stage 2/3 AKI (AKIN 2/3: 16.7% versus AKIN 1: 12.9% versus no AKI: 4.4%; P<0.001), as was AKI requiring dialysis (2.2% versus 1.1% versus 0.2%; P<0.001; Figure 1A through 1F).

The incidence of adverse events was highest within the first 30 days after hospital discharge, irrespective of event or presence or severity of AKI. For the combined outcome of death, MI, and bleeding the highest incidence of events was within the first 30 days (AKIN 2/3: 36.8% of all events, AKIN 1: 26.2% of all events, and no AKI: 19.5%). The same was true for individual events of death (AKIN 2/3: 39.4% of deaths, AKIN 1: 26.7%, and no AKI: 16.6%), MI (AKIN 2/3: 18.2% of MIs, AKIN 1: 19.0%, and no AKI: 21.8%), bleeding (AKIN 2/3: 18.4%, AKIN 1: 23.4%, no AKI: 20.5%), hospitalization for AKI (AKIN 2/3: 33.1%, AKIN 1: 27.6%, no AKI: 19.8%), and AKI requiring dialysis (AKIN 2/3: 45.9%, AKIN 1: 39.8%, no AKI: 28.5%; Figure 2A through 2F; Table II in the Data Supplement).

Adjusted Outcomes

After covariate adjustment, patients having in-hospital AKI were at higher hazard of the primary end point, a composite of post-discharge death, MI, and bleeding at 1 year, as compared with patients who did not develop in-hospital AKI. Hazard of events also increased with severity of in-hospital AKI, with AKIN stage 2/3 in-hospital AKI associated with the highest hazard of death, MI, and bleeding (hazard ratio [HR] 2.13; 95% confidence interval [CI], 2.01–2.26; AKIN stage 1: HR, 1.53; 95% CI, 1.49–1.56; Figure 3). Compared with patients without in-hospital AKI, development of in-hospital AKI was associated with higher rates of individual events of post-discharge mortality (AKIN stage 2/3: HR, 2.52; 95% CI, 2.36–2.70; AKIN stage 1: HR, 1.65; 95% CI, 1.60–1.69), MI (AKIN stage 2/3: HR, 1.29; 95% CI, 1.15–1.45; AKIN stage 1: HR, 1.32; 95% CI, 1.26–1.38), and bleeding (AKIN stage 2/3: HR, 1.40; 95% CI, 1.19–1.66; AKIN stage 1: HR, 1.31; 95% CI, 1.23–1.40). Development of in-hospital AKI was also associated with higher rates of post-discharge rehospitalization for AKI (AKIN stage 2/3: HR, 2.22; 95% CI, 2.04–2.41; AKIN stage 1: HR, 1.70; 95% CI, 1.64–1.76) and AKI requiring dialysis (AKIN stage 2/3: HR, 4.73; 95% CI, 3.73–5.99; AKIN stage 1: HR, 2.59; 95% CI, 2.29–2.92) as compared with those patients who did not develop in-hospital AKI.

Secondary and Sensitivity Analyses

A secondary analysis was performed, evaluating the association between development of post-discharge adverse events and the development of in-hospital AKIN stage 2 and stage 3 renal insufficiency separately, dividing the cohort into 4 categories of renal injury: no AKI, AKIN stage 1, AKIN stage 2, and AKIN stage 3. There were 3689 patients with AKIN stage 2 in-hospital AKI (0.81% of total) and 1954 patients with AKIN stage 3 in-hospital AKI (0.43%). After adjustment, hazard of death, MI, or rehospitalization for bleeding at 1 year remained higher with increasing severity of renal injury. Development of AKIN stage 3 in-hospital AKI carried a similar hazard of death, MI, or bleeding as AKIN stage 2 when compared with patients without AKI, with both significantly higher than AKIN stage 1 (AKIN 3: HR, 2.48; 95% CI, 2.22–2.77; AKIN 2: HR, 2.48; 95% CI, 2.30–2.68; AKIN 1: HR, 1.64; 95% CI, 1.59–1.68). Similarly, patients with AKIN stage 3 in-hospital AKI carried similar hazard of rehospitalization for AKI as AKIN stage 2,

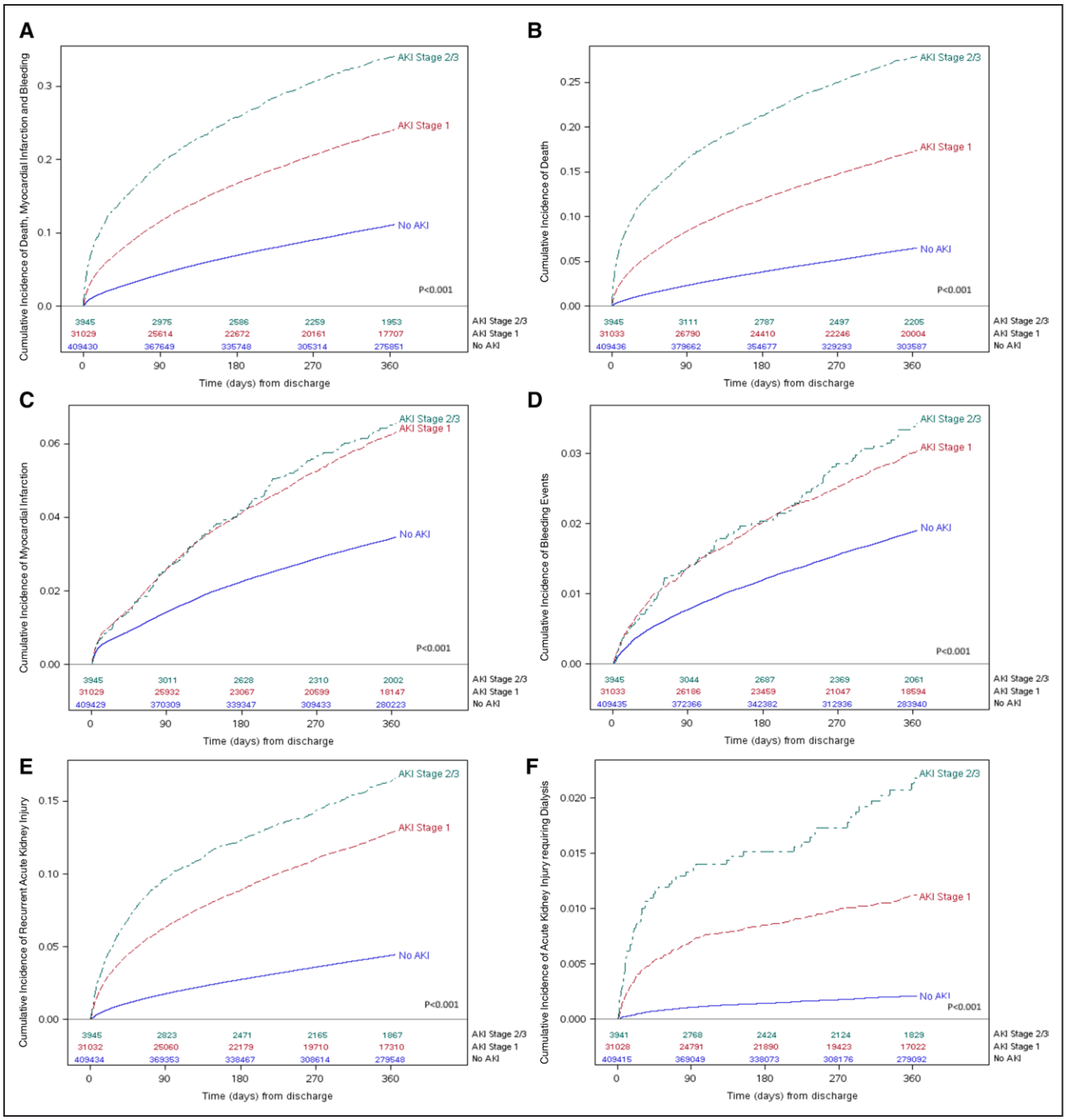

Figure 1. Unadjusted cumulative incidence of adverse events post-discharge, by presence and severity of in-hospital acute kidney injury (AKI). **A**, Death, myocardial infarction, and bleeding; (**B**) death; (**C**) myocardial infarction; (**D**) bleeding events; (**E**) recurrent acute kidney injury; and (**F**) acute kidney injury requiring dialysis.

but both with higher hazard than AKIN1 (AKIN 3: HR, 2.91; 95% CI, 2.46–3.44; AKIN 2: HR, 2.24; 95% CI, 1.99–2.52; AKIN 1: HR, 1.83; 95% CI, 1.76–1.91). Finally, AKIN stage 3 patients had the highest hazard for AKI requiring dialysis, followed by AKIN stage 2 and AKIN stage 1 (AKIN 3: HR, 9.26; 95% CI, 6.07–14.12; AKIN 2: HR, 4.37; 95% CI, 3.18–6.01; AKIN 1: HR, 2.82; 95% CI, 2.42–3.28).

We also compared demographic, clinical, and procedural characteristics of our cohort with those of patients excluded from the analysis because of incomplete periprocedural assessment of renal function (missing periprocedural creatinine values). Patients missing periprocedural assessment of renal function had statistically significantly different but similar ages, sexes, and body mass indices as those included in the analysis. They also had less frequent histories of diabetes mellitus, peripheral or cerebrovascular disease, or previous renal failure. Patients with incomplete renal assessment had higher rates of atypical chest pain, stable angina, or unstable angina as their indication for PCI. Patients with incomplete periprocedural assessment of renal function were less likely

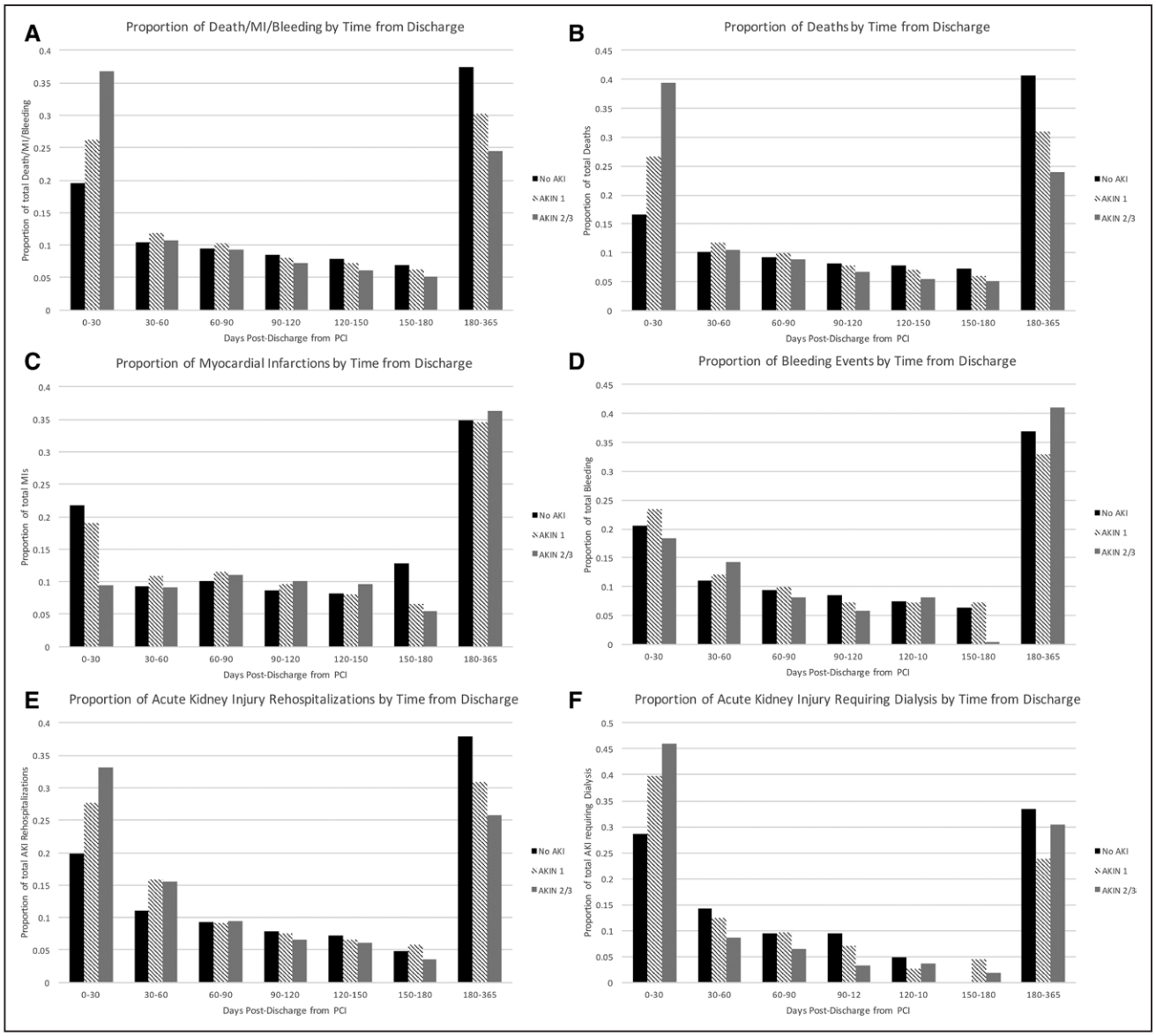

Figure 2. Timing of unadjusted adverse events from hospital discharge, by presence and severity of in-hospital acute kidney injury. **A**, Death, myocardial infarction, and bleeding; (**B**) death; (**C**) myocardial infarction; (**D**) bleeding events; (**E**) recurrent acute kidney injury (AKI); and (**F**) acute kidney injury requiring dialysis. AKIN indicates Acute Kidney Injury Network; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

to present with heart failure, in cardiogenic shock, or require intra-aortic balloon pump placement, underwent multivessel PCI less frequently, and received lower volumes of contrast (Table III in the Data Supplement) as compared with those with complete periprocedural creatinine assessment.

Discussion

In this national, multicenter, real-world cohort of Medicare beneficiaries, we found that AKI remains a common complication after PCI, occurring in 8.8% of those patients with periprocedural assessment of renal function. Furthermore, in-hospital AKI is associated with significant morbidity and mortality after hospital discharge. This analysis demonstrates an association between in-hospital AKI after PCI and higher rates of post-discharge mortality, MI, bleeding-related hospitalization, and recurrence of renal insufficiency at 1 year when compared with patients without in-hospital AKI, with the hazard of adverse events increasing in parallel with the severity of in-hospital AKI as defined by AKIN criteria. Finally, these adverse events occur most frequently in the first 30 days after discharge, suggesting a critical period of vulnerability for patients with AKI after PCI.

Previous work demonstrating an association between inpatient AKI and adverse outcomes has been limited by small cohorts, single-center evaluations, restriction to acute MI or clinical trial populations, or the use of nonstandard definitions of AKI.[3–13] Furthermore, the majority of these studies have focused solely on inpatient events. The few that evaluated long-term risks of AKI demonstrated similar findings of increased risk for cardiovascular events, mortality, and bleeding but did not assess long-term effects on recurrent renal injury. In addition, these studies were performed in varied populations, with

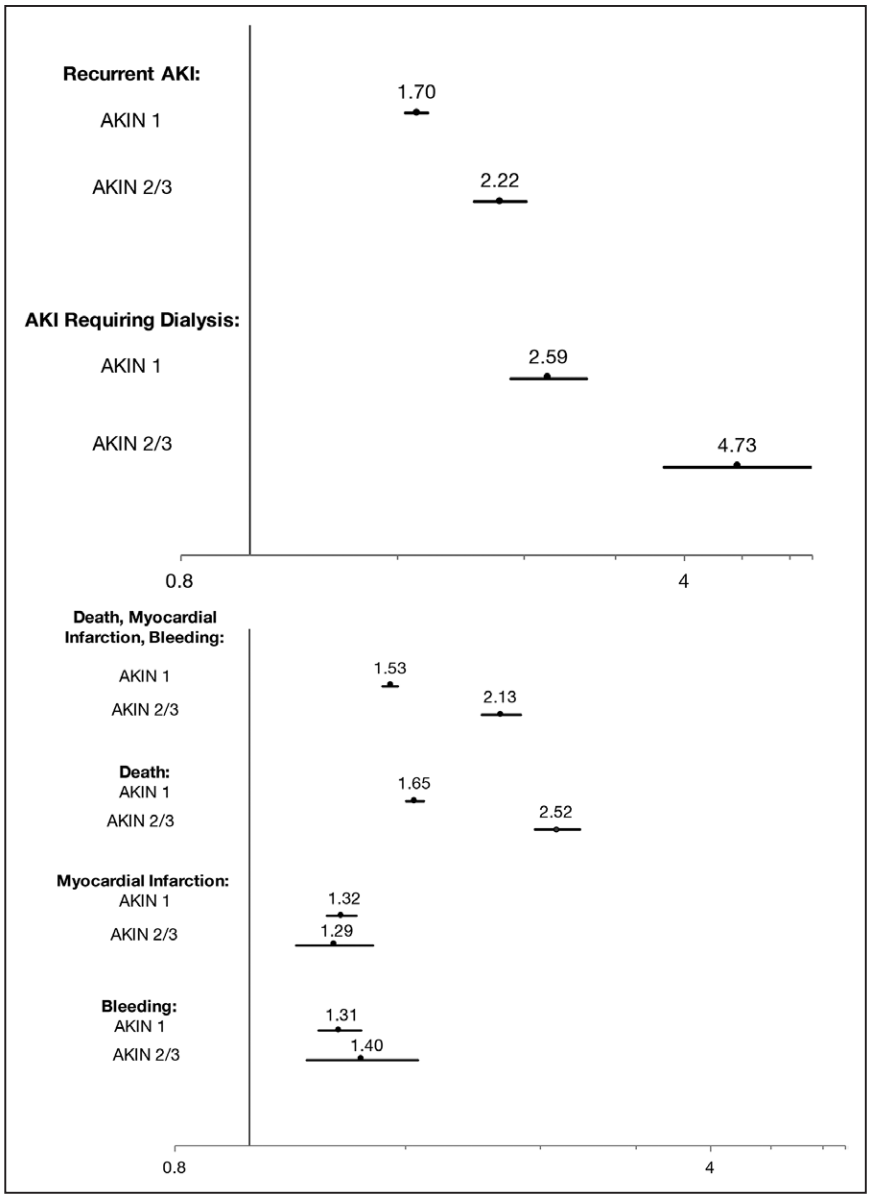

Figure 3. Hazard ratios for adverse events post-discharge, by presence and severity of in-hospital acute kidney injury (AKI). AKIN indicates Acute Kidney Injury Network.

nonstandardized definitions of AKI, and with many occurring before national societal efforts recognizing and raising awareness of the risks associated with post-PCI AKI. Our analysis evaluated all Medicare beneficiaries undergoing PCI with periprocedural creatinine assessment used a recognized and standard definition of AKI and reflects a national experience in the largest evaluation of the association between post-PCI AKI and post-discharge outcomes to date.

Our findings not only add to the body of literature supporting a relationship between post-PCI AKI and adverse outcomes but also suggest that this relationship persists well after hospital discharge. In addition, our analysis demonstrates a novel association between in-hospital AKI and long-term risk for recurrent renal injury. It is possible that although initial clinically apparent renal injury may be transient, subclinical injury may persist and predispose patients to adverse outcomes beyond the initial event. Finally, our findings demonstrate an early separation in the incidence of adverse events among patients having in-hospital post-PCI AKI, suggesting an early period of vulnerability for these patients within the first 30 days after hospital discharge. It is possible that novel, modifiable risk markers beyond the presence of AKI can be identified for targeted intervention in the immediate post-discharge period.

Hazard for mortality and adverse events after AKI have not significantly changed from studies performed before our current awareness of the risks associated with AKI, suggesting an ongoing opportunity to develop possible interventions after the development of AKI to mitigate risk of downstream events. Many have pointed to the lack of modifiable risk factors for the development of contrast-induced AKI, outside of avoiding the procedure itself through more discriminant patient selection.[25,26] However, it remains possible that novel, separate, and most importantly, modifiable risk factors for adverse outcomes exist within those that develop AKI that can serve as targets for intervention, such as more judicious and cautious exposure to potentially nephrotoxic agents like angiotensin receptor blockers or angiotensin-converting enzyme inhibitors

among those with recent AKI.[27] Furthermore, there remains evidence to suggest that a systematic quality improvement intervention to reduce post-PCI AKI can impact not only rates of AKI but also outcomes of mortality and bleeding,[28] suggesting that processes outside of the PCI procedure itself can modulate risk. It is also possible that more proximal evaluation of these patients after discharge or through increased scrutiny of their care and post-discharge management can reduce risk of adverse events after discharge.[25] Further study is needed to identify novel risk factors and better define possible interventions, but defining this population and their high risk in the immediate post-discharge period is an important first step and offers a time period for clinicians to focus on.

This study should be viewed in the context of its limitations. First, AKI was defined by the change in serum creatinine from the most recent measurement before PCI. It is possible that initial creatinine measurements may not have represented a true baseline and may have been affected by hemodynamic instability or other sources of renal injury, reducing the sensitivity of our analysis to the development of AKI within our cohort. This potential misclassification would bias results toward the null, but our findings nevertheless demonstrated significant association between AKI and adverse events. Second, our study cohort relied on the presence of a complete periprocedural assessment of renal function (both pre- and postprocedure assessment of creatinine) to determine the development of in-hospital AKI, and many patients were excluded because of missing values. We compared the characteristics of those patients excluded from our analysis with those included and found that those patients without a complete periprocedural creatinine assessment had significantly less comorbidities, less acuity of presentation for PCI, less contrast use, and lower rates of multivessel PCI. These patients would be less likely to have post-PCI AKI by validated risk models and less likely to have adverse events post-PCI.[24,29] The inclusion of these patients, by risk model estimation, would reduce the overall rate of both AKI and adverse outcomes, increasing the apparent strength of the relationship between development of AKI and adverse events. Therefore, exclusion of these patients likely further biased our results toward the null hypothesis, which further supports the validity of the demonstrated association. Third, adverse events were obtained via the use of billing and administrative data, with the possibility of missing events. We limited our cohort to only fee-for-service Medicare eligible patients, using validated linkage between CMS and NCDR data to minimize this possibility. However, by limiting our cohort to a Medicate population, the findings of this analysis may not be representative of younger patients having AKI after PCI. Fourth, this is an observational study and the findings represent associations that should be viewed as hypothesis generating and should not imply causality. Although we used robust adjustment methods for predictors of post-PCI mortality and adverse events, residual or unmeasured confounding may remain, impacting the associations demonstrated. Fifth, we are unable to capture medication changes in follow-up that may have occurred as a result of the development of AKI, which may have had impact on our findings. Sixth, increased operator awareness of the risks of AKI may have resulted in increased efforts to reduce the incidence of post-PCI AKI. Although these efforts may impact the rate of AKI seen in our analysis, they do not alter the relationship noted. Finally, the patients and hospitals participating in the NCDR may not accurately reflect all PCI performed in the United States. However, the CathPCI registry captures the majority of PCI procedures performed nationally and is the largest repository of PCI data in the United States, reflecting the majority of PCI performed in this country.

In a contemporary cohort of Medicare beneficiaries undergoing PCI within the United States, in-hospital AKI was significantly associated with increased risk of death, MI, bleeding, and recurrent kidney injury after hospital discharge. The majority of these events occurred within 30 days of hospital discharge. Clinicians should be aware of an increased risk of adverse events after hospital discharge among patients having post-PCI AKI, including recurrent renal injury.

Disclosures

None.

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