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Association of Chronic Renal Insufficiency With In-Hospital Outcomes After Percutaneous Coronary Intervention

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Background—The association of chronic renal insufficiency with outcomes after percutaneous coronary intervention (PCI) in the current era of drug-eluting stents and modern antithrombotic therapy has not been well characterized.

Methods and Results—We queried the 2007–2011 Nationwide Inpatient Sample databases to identify all patients aged ≥18 years who underwent PCI. Multivariable logistic regression was used to compare in-hospital outcomes among patients with chronic kidney disease (CKD), patients with end-stage renal disease (ESRD), and those without CKD or ESRD. Of 3 187 404 patients who underwent PCI, 89% had no CKD/ESRD; 8.6% had CKD; and 2.4% had ESRD. Compared to patients with no CKD/ESRD, patients with CKD and patients with ESRD had higher in-hospital mortality (1.4% versus 2.7% versus 4.4%, respectively; adjusted odds ratio for CKD 1.15, 95% CI 1.12 to 1.19, *P*<0.001; adjusted odds ratio for ESRD 2.29, 95% CI 2.19 to 2.40, *P*<0.001), higher incidence of postprocedure hemorrhage (3.5% versus 5.4% versus 6.0%, respectively; adjusted odds ratio for CKD 1.21, 95% CI 1.18 to 1.23, *P*<0.001; adjusted odds ratio for ESRD 1.27, 95% CI 1.23 to 1.32, *P*<0.001), longer average length of stay (2.9 days versus 5.0 days versus 6.4 days, respectively; *P*<0.001), and higher average total hospital charges ($60 526 versus $77 324 versus $97 102, respectively; *P*<0.001). Similar results were seen in subgroups of patients undergoing PCI for acute coronary syndrome or stable ischemic heart disease.

Conclusions—In patients undergoing PCI, chronic renal insufficiency is associated with higher in-hospital mortality, higher postprocedure hemorrhage, longer average length of stay, and higher average hospital charges. (*J Am Heart Assoc*. 2015;4: e002069 doi: 10.1161/JAHA.115.002069)

Key Words: chronic kidney disease • end-stage renal disease • in-hospital mortality • percutaneous coronary intervention • postprocedure hemorrhage

More than 19 million people in the United States are estimated to suffer from chronic renal insufficiency (RI).[1] RI, either in the form of chronic kidney disease (CKD,

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referred to as chronic renal dysfunction not requiring renal replacement therapy) or end-stage renal disease (ESRD, referred to as chronic renal dysfunction requiring renal replacement therapy) is known to be an important risk factor in the development and progression of atherosclerotic coronary artery disease (CAD).[2,3] Percutaneous coronary intervention (PCI) is the most commonly utilized revascularization modality for treatment of CAD both in patients with acute coronary syndromes (ACS) and those with stable ischemic heart disease (SIHD).[4,5] Many clinical studies have demonstrated that patients with CKD and those with ESRD have poor outcomes after PCI, including increased in-hospital and long-term mortality, increased rates of myocardial infarction (MI), and increased bleeding complications relative to patients with preserved renal function.[6,7] However, most of these studies were performed before the introduction of drug-eluting stents (DES) and modern antithrombotic therapy.[8–10] Moreover, major PCI trials have traditionally excluded patients with significant RI.[11] Therefore, there are limited recent data available on outcomes after PCI in patients with RI compared

to those without RI. The purpose of this study was to examine the association of RI with in-hospital outcomes after PCI using a contemporary, unselected, "real-world" cohort of patients included in the Nationwide Inpatient Sample (NIS) databases from 2007 to 2011.

Methods

Data Source

Data were obtained from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization project (HCUP) NIS files between 2007 and 2011. The NIS is the largest publicly available all-payer inpatient care database in the United States and contains discharge-level data provided by states (n=46 in 2011) that participate in the HCUP.[12] The NIS was designed to approximate a 20% stratified sample of all United States community hospitals, representing more than 95% of the national population. Criteria used for stratified sampling of hospitals into the NIS include hospital ownership, patient volume, teaching status, urban or rural location, and geographic region. Discharge weights are provided for each patient discharge record, which allow extrapolation to obtain national estimates.

This study was deemed exempt by the New York Medical College Institutional Review Board because the HCUP-NIS is a publicly available database containing deidentified patient information.

Study Population

We used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) procedure codes 00.66, 36.01, 36.02, 36.05, 36.06, 36.07, and 17.55 to identify all patients aged ≥18 years who underwent PCI. Patients who underwent coronary artery bypass grafting (ICD-9-CM procedure codes 36.1x) during the same admission were excluded. Patients with CKD were identified using ICD-9-CM codes 585.1, 585.2, 585.3, 585.4, 585.5, and 585.9. Patients with ESRD were identified using the diagnosis code for CKD requiring long-term dialysis (585.6), or the procedure code for hemodialysis (39.95) or peritoneal dialysis (54.98) except when dialysis was done for acute kidney injury (AKI; ICD-9-CM diagnosis codes 584.5 to 584.9). The CKD and ESRD groups were mutually exclusive; patients with ICD-9-CM codes both for CKD and ESRD were assigned to the ESRD group and patients with codes for CKD but not ESRD were assigned to the CKD group. This approach has been used by previous studies using the NIS database to accurately identify patients with CKD or ESRD.[13,14] In administrative databases, ICD-9-CM coding for RI has been shown to have a sensitivity of 81.9%, specificity of 98.6%, positive predictive value of

71.2%, and negative predictive value of 99.2%.[15] Patients with ACS were identified using respective ICD-9-CM codes for ST-elevation myocardial infarction (410.0x, 410.1x, 410.2x, 410.3x, 410.4x, 410.5x, 410.6x, 410.8x, and 410.9x) and non-ST-elevation acute coronary syndromes (NSTE-ACS; 411.1 and 410.7x). Patients without diagnosis codes for ACS were considered to have undergone PCI for SIHD.

Outcome Measures

Our primary outcome of interest was all-cause in-hospital mortality defined as "died" during the hospitalization encounter in the NIS database. We used postprocedure hemorrhage, acute ischemic stroke (AIS), average length of stay (LOS), and average total hospital charges as secondary outcomes. The ICD-9-CM codes or HCUP Clinical Classification Software codes used to identify these conditions are provided in Table 1. We also studied the incidence of AKI requiring inpatient hemodialysis in patients with no CKD/ESRD and those with CKD.

Table 1. ICD-9-CM and CCS Codes Used to Identify Comorbidities, In-Hospital Procedures, and Complications

Variable	Source	Code(s)
Comorbidities		
Smoking	ICD-9-CM	V15.82, 305.1
Dyslipidemia	CCS	53
Family history of coronary artery disease	ICD-9-CM	V17.3
Prior myocardial infarction	ICD-9-CM	412
Prior PCI	ICD-9-CM	V45.82
Prior coronary artery bypass surgery	ICD-9-CM	V45.81
Atrial fibrillation	ICD-9-CM	427.31
Carotid artery disease	ICD-9-CM	433.10
Dementia	ICD-9-CM	290.xx, 294.1x, 294.2x, 294.8, 331.0 − 331.12, 331.82, 797
Procedures		
Multivessel PCI	ICD-9-CM	00.41, 00.42, 00.43
Bare metal stent	ICD-9-CM	36.06
Drug-eluting stent	ICD-9-CM	36.07
In-hospital complications		
Postprocedure hemorrhage	ICD-9-CM	998.11, 998.12, 285.1
Acute ischemic stroke	ICD-9-CM	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 437.1, 436

CCS indicates Clinical Classification Software; ICD-9-CM, International Classification of Diseases, Ninth Edition, Clinical Modification; PCI, percutaneous coronary intervention.

Patient and Hospital Characteristics

Baseline patient characteristics used included demographics (age, sex, race, primary expected payer, median household income for patient's ZIP code, weekday versus weekend admission), all Elixhauser comorbidities except chronic renal failure (acquired immune deficiency syndrome, alcohol abuse, deficiency anemia, rheumatoid arthritis/collagen vascular diseases, chronic blood loss anemia, congestive heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes [uncomplicated], diabetes [with chronic complications], drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid and electrolyte disorders, metastatic cancer, other neurologic disorders, obesity, paralysis, peripheral vascular disease, psychosis, pulmonary circulation disorders, solid tumor without metastasis, valvular disease, and weight loss),[16,17] other clinically relevant comorbidities (smoking, dyslipidemia, family history of CAD, prior MI, prior PCI, prior coronary artery bypass grafting, atrial fibrillation, carotid artery disease, and dementia), multivessel PCI, and use of bare metal stents (BMS), DES, or percutaneous transluminal coronary angioplasty (PTCA) alone. A list of ICD-9-CM codes and HCUP Clinical Classification Software codes used to identify baseline characteristics is provided in Table 1. We also included hospital variables such as hospital region (Northeast, Midwest, South, and West), bed size (small, medium, and large), location (rural, urban), and teaching status.

Statistical Analysis

Weighted data were used for all statistical analyses. We initially compared the baseline patient and hospital characteristics between the 3 groups (no CKD/ESRD, CKD, and ESRD) using the Pearson χ^2 test for categorical variables and 1-way ANOVA for continuous variables to identify significant univariate associations. In addition, we used absolute standardized difference (ASD), calculated as the difference in means or proportions divided by a pooled estimate of SD, to compare baseline characteristics between the 3 groups using no CKD/ESRD as the reference group. ASD is not as sensitive to sample size as traditional significance testing, and is useful in identifying meaningful differences.[18] Traditionally, an ASD >10 is considered clinically meaningful. Multivariate logistic regression was then used to compare in-hospital outcomes (in-hospital mortality, postprocedure hemorrhage, and AIS) between patients with CKD and patients with ESRD to those without CKD/ESRD. The regression models adjusted for demographics, hospital characteristics, all Elixhauser and other clinically relevant comorbidities, indication for PCI (ACS or SIHD), multivessel PCI, and utilization of BMS, DES, or PTCA alone. Race/ethnicity data were missing in 18.6% of the study population and therefore is reported in the descriptive

statistics but was not included in the primary regression model. To assess whether race was a potential confounder, we conducted sensitivity analysis after additional adjustment for race in records with available race/ethnicity data. Average LOS and total hospital charges (in patients surviving to hospital discharge) were compared between the study groups using linear regression models. Multivariate logistic regression was also used to compare the incidence of AKI requiring hemodialysis after PCI between the no CKD/ESRD and CKD groups. We also conducted subgroup analysis after stratifying patients into those undergoing PCI for ACS or for SIHD.

Statistical analysis was performed using IBM SPSS Statistics 21.0 (IBM Corp, Armonk, NY). A 2-sided *P* value of <0.05 was used to assess for statistical significance for all analyses. Categorical variables are expressed as percentage and continuous variables as mean±SD. Odds ratio (OR) and 95% CI are used to report the results of logistic regression.

Results

Patient and Hospital Characteristics

Of 3 187 404 patients aged ≥18 years who underwent PCI between 2007 and 2011, 2 837 183 (89%) had no CKD/ESRD, 273 242 (8.6%) had CKD, and 76 979 (2.4%) had ESRD. Patients with CKD were more likely to be older compared to patients with no CKD/ESRD (mean age 71.5 years versus 64.2 years; ASD=64.3). Patients with ESRD were more likely to be women, of African American, Hispanic, or Asian/Pacific Islander descent, as compared to patients with no CKD/ESRD (ASD >10 for all comparisons). Smoking and family history of CAD was more prevalent in patients with no CKD/ESRD compared to patients with CKD or ESRD; whereas atrial fibrillation, congestive heart failure, deficiency anemia, coagulopathy, diabetes mellitus, hypertension, fluid and electrolyte disorders, and peripheral vascular disease were comorbidities more prevalent in patients with CKD or ESRD compared to patients with no CKD/ESRD (ASD >10 for all comparisons) (Table 2).

In-Hospital Outcomes of Patients Undergoing PCI

In the overall study population, 65.3% patients in the no CKD/ESRD group underwent PCI for ACS compared to 66.1% in the CKD group and 60.5% in the ESRD group (ASD <10 for CKD versus no CKD/ESRD and ASD=10.1 for ESRD versus no CKD/ESRD; Table 2). Although patients with CKD had higher observed rates of utilization of multivessel PCI than patients with no CKD/ESRD, this difference was not clinically meaningful (19.6% versus 16.8%; ASD <10). In contrast, patients with ESRD were more likely to undergo multivessel PCI compared to patients with no CKD/ESRD (20.8% versus

Table 2. Baseline Demographics, Hospital Characteristics, and Comorbidities of Patients Undergoing PCI

Variable	Overall	No CKD/ESRD	CKD	ESRD	P Value	Absolute Standardized Difference	
						CKD vs No CKD/ESRD	ESRD vs No CKD/ESRD
Number of cases (weighted)	3 187 404	2 837 183	273 242	76 979			
Age, mean±SD (y)	64.5±12.4	63.9±12.3	71.5±11.3	64.2±11.9	<0.001	64.3	3.2
Women	33.9%	33.5%	35.2%	42.0%	<0.001	3.6	17.5
Race*					<0.001		
White	78.1%	79.2%	74.3%	50.0%		11.6	64.3
African American	8.5%	7.6%	12.0%	25.0%		14.7	48.3
Hispanic	6.7%	6.4%	7.1%	15.1%		2.8	28.2
Asian or Pacific Islander	2.4%	2.3%	2.5%	4.9%		1.7	14.0
Native American	0.7%	0.7%	0.6%	1.2%		1.6	4.9
Other	3.7%	3.7%	3.4%	3.9%		1.6	1.1
Primary expected payer					<0.001		
Medicare	50.8%	47.9%	72.6%	77.6%		52.1	64.5
Medicaid	5.7%	5.8%	5.0%	6.5%		3.6	2.9
Private insurance	34.9%	37.1%	18.0%	13.5%		43.7	56.5
Self-pay	5.2%	5.6%	2.3%	1.1%		17.2	25.4
No charge	0.5%	0.5%	0.3%	0.1%		4.3	9.0
Other	2.9%	3.1%	1.9%	1.3%		7.8	11.9
Median household income					<0.001		
0 to 25th percentile	26.8%	26.4%	28.2%	35.4%		4.1	19.5
26th to 50th percentile	27.0%	27.0%	27.3%	25.0%		0.7	4.6
51st to 75th percentile	24.6%	24.7%	24.2%	22.9%		1.2	4.2
76th to 100th percentile	21.6%	21.9%	20.2%	16.7%		4.0	13.0
Weekend admission	16.2%	16.1%	17.2%	15.9%	<0.001	3.1	0.6
Hospital characteristics							
Region					<0.001		
Northeast	19.1%	19.3%	18.0%	17.6%		3.3	4.2
Midwest	25.8%	25.7%	27.2%	21.4%		3.3	10.2
South	38.5%	38.5%	37.8%	40.3%		1.3	3.7
West	16.7%	16.5%	17.0%	20.7%		1.2	10.7
Bed size†					<0.001		
Small	6.9%	6.9%	7.2%	6.2%		1.1	2.8
Medium	20.0%	20.1%	19.5%	18.9%		1.4	2.9
Large	73.1%	73.0%	73.3%	74.9%		0.6	4.2
Urban location	93.9%	93.8%	94.5%	95.4%	<0.001	2.8	7.0
Teaching hospital	54.7%	54.5%	55.7%	58.5%	<0.001	2.5	8.0
Comorbidities‡							
Smoking	35.8%	37.3%	25.1%	18.0%	<0.001	26.6	44.2
Dyslipidemia	68.0%	68.7%	65.9%	49.6%	<0.001	6.0	39.7
Family history of coronary artery disease	10.2%	10.9%	5.5%	2.8%	<0.001	19.5	32.5
Prior myocardial infarction	13.3%	13.1%	15.7%	13.1%	<0.001	7.5	0.1

Continued

Table 2. Continued

Variable	Overall	No CKD/ESRD	CKD	ESRD	*P* Value	Absolute Standardized Difference	
						CKD vs No CKD/ESRD	ESRD vs No CKD/ESRD
Prior PCI	19.6%	19.5%	20.4%	17.1%	<0.001	2.1	6.2
Prior coronary artery bypass grafting	7.3%	7.0%	10.0%	9.6%	<0.001	10.8	9.7
Atrial fibrillation	9.7%	8.9%	17.2%	14.3%	<0.001	24.7	16.9
Congestive heart failure	15.5%	12.6%	38.5%	42.9%	<0.001	62.3	72.0
Carotid artery disease	1.9%	1.7%	3.3%	1.9%	<0.001	9.9	1.2
Dementia	0.6%	0.5%	1.3%	0.7%	<0.001	7.7	2.6
Acquired immune deficiency syndrome	0.1%	0.1%	0.1%	0.4%	<0.001	0.4	5.1
Alcohol abuse	2.0%	2.1%	1.2%	0.7%	<0.001	7.5	11.7
Deficiency anemia	8.8%	6.2%	25.6%	45.2%	<0.001	55.2	99.8
Rheumatoid arthritis/collagen vascular diseases	1.8%	1.8%	2.4%	1.7%	<0.001	4.7	0.2
Chronic blood loss anemia	0.5%	0.4%	1.2%	1.0%	<0.001	8.9	6.8
Chronic pulmonary disease	15.7%	15.0%	21.8%	17.8%	<0.001	17.6	7.5
Coagulopathy	2.1%	1.8%	4.3%	6.1%	<0.001	14.4	22.1
Depression	5.7%	5.7%	6.3%	6.2%	<0.001	2.7	2.3
Diabetes mellitus (uncomplicated)	29.9%	28.9%	37.7%	35.4%	<0.001	18.7	13.9
Diabetes mellitus (complicated)	4.0%	2.3%	15.0%	29.6%	<0.001	46.5	80.5
Drug abuse	1.3%	1.4%	0.9%	1.1%	<0.001	4.3	2.2
Hypertension	70.9%	69.0%	85.3%	88.7%	<0.001	39.6	49.6
Hypothyroidism	8.1%	7.6%	12.1%	10.1%	<0.001	15.1	8.7
Liver disease	0.9%	0.8%	1.3%	2.3%	<0.001	5.1	11.8
Lymphoma	0.3%	0.3%	0.6%	0.5%	<0.001	4.2	3.2
Fluid and electrolyte disorder	9.3%	7.8%	20.2%	26.2%	<0.001	36.5	50.6
Metastatic cancer	0.3%	0.3%	0.5%	0.3%	<0.001	2.9	0.3
Other neurologic disorders	3.1%	2.9%	4.2%	4.9%	<0.001	7.1	10.2
Obesity	12.6%	12.4%	15.1%	11.3%	<0.001	8.0	3.3
Paralysis	0.7%	0.6%	1.4%	1.8%	<0.001	7.8	10.8
Peripheral vascular disease	10.8%	9.6%	20.5%	23.1%	<0.001	31.1	37.3
Psychoses	1.4%	1.3%	1.5%	1.8%	<0.001	1.7	3.5
Pulmonary circulation disorders	0.2%	0.1%	0.4%	0.8%	<0.001	5.7	9.7
Solid tumor without metastasis	0.9%	0.9%	1.4%	0.7%	<0.001	4.5	1.7
Valvular disease	0.3%	0.2%	0.7%	1.2%	<0.001	6.7	11.5
Weight loss	0.8%	0.7%	1.8%	3.8%	<0.001	10.6	21.4
Indication for PCI					<0.001		
Acute coronary syndrome	65.3%	65.3%	66.1%	60.5%		1.6	10.1
Stable ischemic heart disease	34.7%	34.7%	33.9%	39.5%		1.6	10.1

CKD indicates chronic kidney disease; ESRD, end-stage renal disease; PCI, percutaneous coronary intervention.

*Race data provided for records with available race/ethnicity information (n=2 593 592 for overall PCI population, n=2 299 229 for no CKD/ESRD group, n=228 096 for CKD group, n=66 277 for ESRD group).

†Numbers of beds categories are specific to hospital location and teaching status, available at http://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

‡Comorbidities were extracted from the database using International Classification of Diseases, Ninth Edition, Clinical Modification Diagnosis or Clinical Classification Software codes.

16.8%; ASD=10.1). Patients with CKD had similar rates of utilization of BMS (28.6% versus 25.7%), DES (63.7% versus 67.7%), and PTCA alone (7.7% versus 6.5%) as compared to patients with no CKD/ESRD (ASD <10 for all comparisons). In contrast, patients with ESRD were less likely to receive DES (60.3% versus 67.7%; ASD=15.7), more likely to undergo PTCA alone (10.7% versus 6.5%; ASD=14.8), and had similar likelihood of receiving BMS (29.1% versus 25.7%; ASD <10) as compared to patients with no CKD/ESRD.

Unadjusted analysis showed that compared to patients with no CKD/ESRD, those with CKD or ESRD had significantly higher in-hospital mortality (1.4% versus 2.7% versus 4.4%, respectively; unadjusted OR for CKD 1.98, 95% CI 1.93 to 2.03, $P<0.001$; unadjusted OR for ESRD 3.31, 95% CI 3.19 to 3.43, $P<0.001$). Even after adjustment for demographics, hospital characteristics, comorbidities, indication for PCI (ACS or SIHD), multivessel PCI, and utilization of BMS, DES, or PTCA alone, patients with CKD and patients with ESRD had higher in-hospital mortality compared to those without CKD/ESRD (adjusted OR for CKD 1.15, 95% CI 1.12 to 1.19, $P<0.001$; adjusted OR for ESRD 2.29, 95% CI 2.19 to 2.40, $P<0.001$). Similar results were obtained with sensitivity

analysis after additional adjustment for race in patients with available race/ethnicity data (Table 3).

Compared to patients with no CKD/ESRD, patients with CKD and patients with ESRD had a higher incidence of postprocedure hemorrhage (3.5% versus 5.4% versus 6.0%, respectively; adjusted OR for CKD 1.21, 95% CI 1.18 to 1.23, $P<0.001$; adjusted OR for ESRD 1.27, 95% CI 1.23 to 1.32, $P<0.001$), higher incidence of AIS (0.5% versus 0.9% versus 1.1%, respectively; adjusted OR for CKD 1.08, 95% CI 1.03 to 1.14, $P=0.002$; adjusted OR for ESRD 1.17, 95% CI 1.08 to 1.27, $P<0.001$), longer average LOS (2.9 days versus 5.0 days versus 6.4 days, respectively; $P<0.001$), and higher average total hospital charges ($60 526 versus $77 324 versus $97 102, respectively; $P<0.001$) (Table 3).

In the ACS subgroup, compared to patients with no CKD/ESRD, patients with CKD and patients with ESRD were less likely to have ST-elevation myocardial infarction (34.5% versus 22.3% versus 16.6%) and were more likely to have NSTE-ACS (65.5% versus 77.7% versus 83.4%), ASD=27.4 for CKD versus no CKD/ESRD and ASD=42 for ESRD versus CKD/ESRD. When data were analyzed separately according to the clinical presentation, compared to patients with no CKD/ESRD,

Table 3. In-Hospital Outcomes of Patients Undergoing PCI

In-Hospital Outcomes	Overall	No CKD/ESRD	CKD	ESRD
Number of cases (weighted)	3 187 404	2 837 183	273 242	76 979
In-hospital mortality				
%	1.6	1.4	2.7	4.4
Unadjusted OR (95% CI)	—	Reference	1.98 (1.93 to 2.03)	3.31 (3.19 to 3.43)
Adjusted OR* (95% CI)	—	Reference	1.15 (1.12 to 1.19)	2.29 (2.19 to 2.40)
Adjusted OR† (95% CI)	—	Reference	1.16 (1.12 to 1.20)	2.39 (2.27 to 2.50)
Postprocedure hemorrhage				
%	3.7	3.5	5.4	6.0
Unadjusted OR (95% CI)	—	Reference	1.61 (1.58 to 1.64)	1.78 (1.73 to 1.84)
Adjusted OR* (95% CI)	—	Reference	1.21 (1.18 to 1.23)	1.27 (1.23 to 1.32)
Adjusted OR† (95% CI)	—	Reference	1.22 (1.20 to 1.25)	1.31 (1.27 to 1.36)
Acute ischemic stroke				
%	0.5	0.5	0.9	1.1
Unadjusted OR (95% CI)	—	Reference	1.98 (1.90 to 2.07)	2.48 (2.31 to 2.65)
Adjusted OR* (95% CI)	—	Reference	1.08 (1.03 to 1.14)	1.17 (1.08 to 1.27)
Adjusted OR† (95% CI)	—	Reference	1.00 (0.95 to 1.06)	1.09 (1.00 to 1.19)
Mean length of stay‡	3.1 days	2.9 days	5.0 days	6.4 days
Average hospital charges‡	$62 789	$60 526	$77 234	$97 102

CI indicates confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

*Adjusted for demographics, hospital characteristics, comorbidities, indication for PCI (ST-elevation myocardial infarction, non-ST-elevation acute coronary syndrome, or stable ischemic heart disease), multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

†Sensitivity analysis with additional adjustment for Race in records with available race/ethnicity data (n=2 593 592).

‡Mean length of stay and average hospital charges reported in patients surviving to hospital discharge.

Table 4. In-Hospital Outcomes of Patients With Acute Coronary Syndromes Undergoing PCI

In-Hospital Outcomes	Overall	No CKD/ESRD	CKD	ESRD
Number of cases (weighted)	2 080 690	1 853 549	180 596	46 545
In-hospital mortality				
%	2.2	1.9	3.6	6.1
Unadjusted OR (95% CI)	—	Reference	1.86 (1.81 to 1.91)	3.30 (3.17 to 3.43)
Adjusted OR* (95% CI)	—	Reference	1.11 (1.07 to 1.14)	2.24 (2.13 to 2.35)
Adjusted OR† (95% CI)	—	Reference	1.12 (1.08 to 1.16)	2.36 (2.24 to 2.48)
Postprocedure hemorrhage				
%	4.1	3.9	6.0	6.7
Unadjusted OR (95% CI)	—	Reference	1.57 (1.54 to 1.61)	1.76 (1.70 to 1.83)
Adjusted OR* (95% CI)	—	Reference	1.21 (1.18 to 1.23)	1.26 (1.21 to 1.32)
Adjusted OR† (95% CI)	—	Reference	1.21 (1.18 to 1.24)	1.28 (1.22 to 1.34)
Acute ischemic stroke				
%	0.6	0.5	1.1	1.3
Unadjusted OR (95% CI)	—	Reference	1.97 (1.88 to 2.07)	2.48 (2.28 to 2.69)
Adjusted OR* (95% CI)	—	Reference	1.09 (1.03 to 1.15)	1.14 (1.04 to 1.26)
Adjusted OR† (95% CI)	—	Reference	1.00 (0.94 to 1.06)	1.01 (0.91 to 1.12)
Mean length of stay‡	3.6 days	3.3 days	5.4 days	7.2 days
Average hospital charges‡	$66 759	$64 417	$81 525	$105 819

CI indicates confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

*Adjusted for demographics, hospital characteristics, comorbidities, presentation (ST-elevation or non-ST-elevation acute coronary syndrome), multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

†Sensitivity analysis with additional adjustment for Race in records with available race/ethnicity data (n=1 699 229).

‡Mean length of stay and average hospital charges reported in patients surviving to hospital discharge.

patients with CKD and patients with ESRD had higher in-hospital mortality both in the ACS (1.9% versus 3.6% versus 6.1%; adjusted OR for CKD 1.11, 95% CI 1.07 to 1.14, *P*<0.001; adjusted OR for ESRD 2.36, 95% CI 2.24 to 2.48, *P*<0.001) and the SIHD (0.3% versus 1.0% versus 1.8%; adjusted OR for CKD 1.39, 95% CI 1.27 to 1.51, *P*<0.001; adjusted OR for ESRD 2.36, 95% CI 2.10 to 2.64, *P*<0.001) subgroups. Compared to patients with no CKD/ESRD, patients with CKD or ESRD had higher postprocedure hemorrhage, longer average LOS, and higher average total hospital charges, irrespective of whether PCI was performed for ACS or for SIHD. Sensitivity analysis after additional adjustment for race in patients with available race/ethnicity data showed similar results (Tables 4 and 5).

AKI Requiring Inpatient Dialysis

Compared to patients with no CKD/ESRD, patients with CKD had an ≈6-fold risk of developing AKI requiring dialysis during the hospitalization (1.4% versus 0.1%; adjusted OR 5.54, 95% CI 5.22 to 5.88, *P*<0.001). Similar results were seen both in the ACS and in SIHD subgroups (Table 6).

Discussion

In the current study, we observed that patients with CKD and patients with ESRD had significantly higher prevalence of most cardiovascular comorbidities compared to patients with no CKD/ESRD. However, even after adjustment for these baseline differences, patients with CKD and patients with ESRD still had higher in-hospital mortality, hemorrhagic complications, AIS, and longer average LOS, suggesting that RI continues to be an independent predictor of adverse outcomes after PCI in the era of widespread use of DES and modern antiplatelet and antithrombotic therapies. RI was associated with adverse in-hospital outcomes irrespective of whether PCI was performed for ACS or for SIHD. Also, we observed a gradient of risk for all adverse outcomes, with CKD patients having worse outcomes than patients without CKD/ESRD, and ESRD patients having the least favorable outcomes.

Prior investigations with smaller study populations have also reported worse in-hospital and long-term outcomes after PCI in patients with RI.[6,19,20] In one of the earliest such studies, Rubenstein et al[6] compared outcomes of 362 CKD patients (CKD defined as serum creatinine >1.5 mg/dL) with 2972

Table 5. In-Hospital Outcomes of Patients With Stable Ischemic Heart Disease Undergoing PCI

In-Hospital Outcomes	Overall	No CKD/ESRD	CKD	ESRD
Number of cases (weighted)	1 106 714	983 634	92 646	30 434
In-hospital mortality				
%	0.4	0.3	1.0	1.8
Unadjusted OR (95% CI)	—	Reference	3.24 (3.01 to 3.49)	5.94 (5.42 to 6.52)
Adjusted OR* (95% CI)	—	Reference	1.39 (1.27 to 1.51)	2.36 (2.10 to 2.64)
Adjusted OR† (95% CI)	—	Reference	1.31 (1.19 to 1.44)	2.32 (2.05 to 2.63)
Postprocedure hemorrhage				
%	2.8	2.6	4.4	5.0
Unadjusted OR (95% CI)	—	Reference	1.69 (1.64 to 1.75)	1.94 (1.84 to 2.05)
Adjusted OR* (95% CI)	—	Reference	1.18 (1.14 to 1.23)	1.23 (1.16 to 1.31)
Adjusted OR† (95% CI)	—	Reference	1.22 (1.17 to 1.28)	1.33 (1.25 to 1.42)
Acute ischemic stroke				
%	0.4	0.3	0.6	0.8
Unadjusted OR (95% CI)	—	Reference	1.99 (1.82 to 2.17)	2.70 (2.38 to 3.07)
Adjusted OR* (95% CI)	—	Reference	1.04 (0.94 to 1.15)	1.21 (1.04 to 1.41)
Adjusted OR† (95% CI)	—	Reference	0.99 (0.89 to 1.11)	1.28 (1.09 to 1.50)
Mean length of stay‡	2.3 days	2.1 days	4.1 days	5.2 days
Average hospital charges‡	$55 473	$53 331	$69 103	$84 362

CI indicates confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

*Adjusted for demographics, hospital characteristics, comorbidities, multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

†Sensitivity analysis with additional adjustment for Race in records with available race/ethnicity data (n=894 362).

‡Mean length of stay and average hospital charges reported in patients surviving to hospital discharge.

patients with normal renal function who underwent PCI between 1994 and 1997. Patients with CKD had reduced procedural success and greater in-hospital combined major events (death, Q-wave MI, or emergent coronary artery bypass grafting). Subsequently, even milder forms of CKD were shown to be associated with worse outcomes after PCI.[21,22] However, these studies were performed before the widespread use of DES and routine utilization of dual antiplatelet and modern antithrombotic therapies. Our study, performed in the era of newer-generation stents and modern adjunctive medical therapies, reaffirms the association of CKD and ESRD with adverse in-hospital outcomes after PCI. There is some evidence that DES utilization can improve outcomes in patients with RI undergoing PCI compared with BMS. Jeong et al[23] compared 1-year outcomes in patients with moderate CKD (defined as estimated creatinine clearance <60 mL/min) treated with DES versus those treated with BMS. Compared to BMS, DES utilization was associated with lower 1-year major adverse cardiac events (cardiac death, nonfatal MI, or target vessel revascularization). Other studies have also shown that DES use may be associated with lower rates of long-term angiographic restenosis and clinical adverse events in patients with significant RI.[24,25] Despite this, our results indicate that

patients with RI are less likely to undergo DES implantation and are more likely to receive BMS or PTCA alone.

Mechanisms by which RI influences mortality and other adverse cardiovascular events after PCI are not completely understood. As observed in previous reports[6,21,26] and the current study, patients with RI comprise a high-risk population with much greater prevalence of comorbidities. RI has also been associated with increased inflammation, oxidative stress, hyperparathyroidism, increased calcium-phosphate product, hyperhomocysteinemia, dyslipidemia, insulin resistance, and decreased nitric oxide activity.[27,28] These pathophysiological changes that occur with RI are associated with endothelial dysfunction and accelerated atherosclerosis,[28] which may contribute to more diffuse CAD, more calcified plaques, and, therefore, lower procedural success after PCI in patients with RI. RI has been shown to be an important risk factor in the occurrence and progression of coronary calcification,[29] which, in turn, has been associated with increased rates of all-cause mortality, cardiac death, stent thrombosis, and target vessel revascularization in patients undergoing PCI.[30] Osten et al[20] indeed showed that patients with RI undergoing PCI had lower procedural success rates, more frequent failure of stent delivery, and greater post-PCI residual stenosis compared with

Table 6. Acute Kidney Injury Requiring Inpatient Hemodialysis in Patients Undergoing PCI

Acute Kidney Injury Requiring Dialysis	No CKD/ESRD	CKD
Overall PCI		
%	0.1	1.4
Unadjusted OR (95% CI)	Reference	15.55 (14.80 to 16.34)
Adjusted OR* (95% CI)	Reference	5.54 (5.22 to 5.88)
Adjusted OR† (95% CI)	Reference	5.63 (5.28 to 6.00)
PCI for acute coronary syndromes		
%	0.1	1.7
Unadjusted OR (95% CI)	Reference	14.01 (13.28 to 14.78)
Adjusted OR‡ (95% CI)	Reference	5.05 (4.73 to 5.39)
Adjusted OR† (95% CI)	Reference	5.09 (4.75 to 5.46)
PCI for stable ischemic heart disease		
%	0.02	0.8
Unadjusted OR (95% CI)	Reference	27.96 (24.37 to 32.08)
Adjusted OR§ (95% CI)	Reference	9.03 (7.71 to 10.58)
Adjusted OR† (95% CI)	Reference	9.58 (8.10 to 11.33)

CI indicates confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; OR, odds ratio; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.

*Adjusted for demographics, hospital characteristics, comorbidities, indication for PCI (ST-elevation acute coronary syndrome, non-ST-elevation acute coronary syndrome, or stable ischemic heart disease), multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

†Sensitivity analysis after additional adjustment for Race in records with available race/ethnicity data.

‡Adjusted for demographics, hospital characteristics, comorbidities, presentation (ST-elevation or non-ST-elevation acute coronary syndrome), multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

§Adjusted for demographics, hospital characteristics, comorbidities, multivessel PCI, and utilization of bare metal stents, drug-eluting stents, or PTCA alone.

those with normal renal function. These findings were attributed to more complex and heavily calcified anatomy in patients with RI. Another potential reason for higher mortality after PCI in patients with RI could be higher incidence of malignant tachyarrhythmias after revascularization in these patients.[31] Increased susceptibility to arrhythmias in patients with RI has been attributed to increased sympathetic activity, intermittent volume overload, fluid and electrolyte disturbances, left ventricular hypertrophy, electrophysiological changes of the myocardium, renal anemia, and a generalized inflammatory state.[32–34] In addition, multiple studies have shown that utilization of guideline-recommended adjunctive cardiovascular medications such as dual antiplatelet therapy, β-blockers, angiotensin-converting enzyme inhibitors, and statins decreases with increasing severity of RI.[35,36] The above mechanisms, in conjunction, likely contribute to increased mortality after PCI in patients with RI.

Our findings of increased incidence of postprocedure hemorrhage after PCI in patients with CKD and patients with ESRD as compared to patients with no CKD/ESRD are consistent with those of previous studies.[20,37,38] The increased risk of hemorrhagic complications in patients with RI undergoing PCI can partly be explained by several inherent abnormalities of primary hemostasis in these patients, particularly platelet dysfunction characterized by decreased release of adenosine triphosphate and decreased serotonin content in dense granules.[39] Additionally, it has been shown that estimation of renal function based on serum creatinine alone sometimes can lead to inadvertent overestimation of renal function resulting in overdosing of antithrombotic medications that are renally metabolized. RI has indeed been shown to be an independent predictor of excessive dosing of heparin and glycoprotein IIb/IIIa inhibitors among patients with ACS.[40,41] RI has also been associated with higher incidence of complications such as retroperitoneal hematoma and femoral artery thrombosis with the use of vascular closure devices following PCI.[42]

Concordant with results of previous studies,[38] we found that patients with RI had longer average LOS after PCI irrespective of whether PCI was performed for ACS or for SIHD. Besides increased rates of bleeding complications, other factors, which could have contributed to longer LOS in patients with RI, include increased risk of both ischemic complications such as postprocedure MI, stent thrombosis, target vessel or nontarget vessel revascularization,[43] and local access site complications.[44] Additional factors that could be associated with longer LOS in patients with RI include an increased risk of contrast-induced nephropathy in patients with CKD[45] and need for dialysis after PCI in patients with ESRD.

Periprocedural AIS after PCI is a rare complication but has been associated with exceedingly high in-hospital mortality of ≈20%.[46] The finding of CKD and ESRD being independently associated with the risk of AIS after PCI in the overall study population and in those undergoing PCI for ACS in an important finding of our study. Although this association was no longer statistically significant after adjusting for race/ethnicity, this may have been due to the large proportion of missing data on race/ethnicity in our study. AKI requiring dialysis is a known complication after PCI and is associated with increased risk of postprocedural MI, bleeding, and death.[9,47] Consistent with results of previous reports,[47] our study shows that patients with underlying CKD have a multifold risk of developing AKI requiring dialysis than those without CKD.

Study Limitations

This study has certain limitations. Healthcare data can typically be derived from administrative databases or clinical databases, the latter including retrospective chart abstraction

and prospectively maintained registries. Administrative databases, typically obtained from discharge billing records, are an inexpensive and readily accessible source of information regarding acute care hospitalizations.[48] Some of the limitations of administrative databases include errors in diagnosis or procedure coding,[49] restricted study populations (eg, Medicare Coverage Databases, Veterans Administration Databases),[50] lack of critical clinical variables,[51] and potential for inaccurate differentiation of comorbidities from complications.[52] Additionally, most administrative databases record only all-cause in-hospital mortality, and causes of death are not differentiated. On the other hand, some of the limitations of clinical registries include participation of only selected hospitals, variability in data definitions, interpretation, abstraction and collection intervals, and lack of information on hospital charges and costs. The large sample size and the ability to obtain national estimates based on the provided discharge weights are important strengths of the NIS database. Our study also has the inherent possibility of selection bias associated with its retrospective, observational design. Although we adjusted for multiple baseline characteristics, there is a potential for residual measured or unmeasured confounding. We could not calculate estimated glomerular filtration rates given the lack of availability of laboratory data; therefore, results could not be stratified according to stage of CKD. Detailed angiographic data such as reference vessel diameter, lesion length, lesion type, procedural success, etc. were not available. Since there was no information available on utilization of transfemoral versus transradial access, we could not compare the effect of these approaches on the incidence of postprocedure hemorrhage. There were no data available either on the use of glycoprotein IIb/IIIa inhibitors during PCI or on the use of different antithrombotic medications (unfractionated or low molecular weight heparin, fondaparinux, or bivalirudin). Therefore, we could not assess whether differential utilization of these medical therapies contributed to worse outcomes after PCI in patients with RI. Lastly, outcomes in NIS are limited to in-hospital events and follow-up data are not available.

Conclusions

In this large nationwide study, we observed that patients with CKD and patients with ESRD had higher in-hospital mortality, higher hemorrhagic complications, longer average LOS, and higher average hospital charges after undergoing PCI as compared to patients with no CKD/ESRD. Patients with CKD and patients with ESRD had worse in-hospital outcomes irrespective of whether PCI was performed for ACS or for SIHD. Awareness of this is crucial in risk stratification of patients undergoing PCI. When patients with RI undergo PCI,

utmost attention is required to optimize outcomes, including accurate dosing of proven medical therapies. Future research should focus on developing strategies to improve outcomes after PCI in patients with RI.

Disclosures

Dr Bhatt discloses the following relationships—Advisory Board: Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care; Chair: American Heart Association Get With The Guidelines Steering Committee; Data Monitoring Committees: Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Associate Editor; Section Editor, Pharmacology), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor); Research Funding: Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi Aventis, The Medicines Company; Unfunded Research: FlowCo, PLx Pharma, Takeda. Dr Fonarow, reports consulting with Astra Zeneca, Bayer, Janssen, and Novartis. All others have no conflicts of interests to disclose.

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