ORIGINAL RESEARCH

Non–ST-Segment–Elevation Myocardial Infarction Among Patients With Chronic Kidney Disease: A Propensity Score–Matched Comparison of Percutaneous Coronary Intervention Versus Conservative Management

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***Background*—**Chronic kidney disease (CKD) remains an independent predictor of cardiovascular morbidity and mortality. CKD complicates referral for percutaneous coronary intervention (PCI) in non–ST-segment–elevation myocardial infarction (NSTEMI) patients because of the risk for acute kidney injury and the need for dialysis, with American College of Cardiology/American Heart Association guidelines underscoring the limited data on these patients.

***Methods and Results*—**Using the National Inpatient Sample to analyze hospitalizations in the United States from 2004 to 2014, we sought to assess PCI utilization and in-hospital outcomes in NSTEMI admissions with CKD. NSTEMI admissions were identified by *International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM)* code 410.7. CKD admissions were identified by *ICD-9-CM* code 585. Propensity score–matched cohorts of patients with NSTEMI were matched for age, sex, comorbidities, race, median household income, primary payer status, and hospital characteristics. Of 4 488 795 hospitalizations for NSTEMI, 31% underwent PCI. Overall, 89% of admissions had no CKD. In addition, 32% of NSTEMI admissions with no CKD and 23%, 14%, and 22% with CKD stages 3, 4, and 5 underwent PCI, respectively. Hospitalized NSTEMI patients with CKD stages 4 and 5 had 41% and 20% less likelihood, respectively, of undergoing PCI compared with those with no CKD. Among hospitalized NSTEMI patients with no CKD or CKD stage 3, 4, or 5, PCI-treated groups had 63%, 57%, 39%, and 59% lower likelihood, respectively, of all-cause, in-hospital mortality compared with propensity score–matched medically managed groups.

***Conclusions*—**PCI use decreased among hospitalized NSTEMI patients as CKD severity increased, and all-cause, in-hospital mortality was greater for NSTEMI patients admitted with more severe CKD regardless of treatment strategy. **(*J Am Heart Assoc.* 2018;7:e007920. DOI: 10.1161/JAHA.117.007920.)**

Key Words: acute coronary syndrome • chronic kidney disease

Chronic kidney disease (CKD) is an independent predictor of poor cardiovascular outcomes.[1,2] Patients with CKD have accelerated atherosclerosis and an increased risk of myocardial infarction, with cardiovascular disease remaining the most common cause of death.[3] Based on previous seminal studies,[4–6] the 2014 American College of Cardiology/American Heart Association (ACC/AHA) and the 2015 European Society of Cardiology guidelines recommend an urgent invasive strategy in high-risk patients presenting with non–ST-segment–elevation myocardial infarction (NSTEMI).[7,8] However, CKD patients are often denied invasive coronary angiography and percutaneous coronary intervention (PCI) because of concerns about acute kidney injury accelerating their progression to dialysis.[9,10] In addition, patients with advanced CKD (stages 4 and 5) have been excluded routinely from most large randomized controlled trials (RCTs) of PCI in acute coronary syndrome.[11,12] This is especially relevant because even mildly abnormal renal function has been independently associated with adverse outcomes following NSTEMI.[1,2] RCTs of PCI are not feasible in this population given the lack of clinical equipoise and multicomorbidity, and

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Accompanying Tables S1 through S6 are available at http://jaha.ahajournals.org/content/7/6/e007920/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- Non–ST-segment–elevation myocardial infarction patients treated with percutaneous coronary intervention have less likelihood of all-cause, in-hospital mortality compared with propensity score–matched medically managed groups across all chronic kidney disease subgroups.

What Are the Clinical Implications?

- Although increasing severity of chronic kidney disease is associated with poor in-hospital outcomes among patients with non–ST-segment–elevation myocardial infarction, percutaneous coronary intervention likely reduces in-hospital mortality among these patients across all chronic kidney disease stages compared with medical management only.

thus we performed a national propensity score–matched analysis to better understand the role of PCI for CKD patients presenting with NSTEMI. The aims of the study were to examine national trends in PCI use among CKD patients hospitalized for NSTEMI and to assess all-cause, in-hospital mortality in propensity score–matched NSTEMI patients with CKD treated with either PCI or medical therapy. We hypothesized that PCI use among NSTEMI patients with CKD would be associated with lower all-cause, in-hospital mortality.

Methods

The data and study materials are publicly available, and the analytic methods will be made available to other researchers on request, by contacting the corresponding author, for purposes of reproducing the results or replicating the procedure. The full data set is available at the Healthcare Cost and Utilization Project and National Inpatient Sample (NIS).[13]

Data Sources and Study Population

This study involved a population-based sample of patients with NSTEMI and CKD who were admitted to hospitals in 46 states from 2004 to 2014. The 2004–2014 NIS is a set of hospital inpatient databases collected by the Healthcare Cost and Utilization Project. The NIS is the largest publicly available, all-payer, inpatient-care database with discharge data from >1200 hospitals, a stratified sample of 20% of all US hospital discharges.[13] These data include primary and secondary admission diagnoses, primary and secondary procedures, admission and discharge status, demographic information (eg, sex, age, race and ethnicity, ZIP code–derived median income, and length of stay), hospital region, teaching status, and bed size.[14] The study was exempted from institutional review board approval, and the requirement for informed consent was waived because the database uses previously collected deidentified data.

Data Extraction and Study Design

Diagnoses and procedures were identified from the *International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM)* diagnostic codes. Our sample included individuals who were admitted with a principal diagnosis of NSTEMI, identified by *ICD-9-CM* code 410.7. We excluded patients with age <18 years and missing information on age, sex, or mortality. We also excluded patients with CKD stage 1 and 2 (glomerular filtration rate >60 mL/min/1.73m^2) because coding for CKD stages 1 and 2 in the hospital setting has been found to be insensitive.[15] CKD patients and end-stage renal disease (ESRD) patients were identified within the NSTEMI subset by *ICD-9-CM* code 585.X in the secondary diagnosis field. Patients on dialysis were identified by *ICD-9-CM* code 39.95 (hemodialysis) and 54.98 (peritoneal dialysis) in either the primary or secondary field. PCI was identified by *ICD-9-CM* code 36.06 or 36.07 in either the primary or secondary field. The study population was divided into 4 groups: (1) no CKD; (2) CKD stage 3; (3) CKD stage 4; and (4) CKD stage 5, ESRD, or dialysis (hemodialysis or peritoneal dialysis). Patients who went on dialysis because of acute kidney injury (AKI), *ICD-9-CM* code 584.X, were not included in group 4. In previous administrative databases, *ICD-9-CM* coding of chronic renal insufficiency has been shown to have sensitivity of 81.9%, specificity of 98.6%, positive predictive value of 71.2%, and negative predictive value of 99.2%.[16] Baseline comorbidities were identified, and comorbidity index was used with methods described by Elixhauser et al.[17]

Statistical Analyses

Univariate and distributional analysis included measures of central tendency, kurtosis, and skew. Bivariate comparisons, such as those comparing the patient characteristics and in-hospital mortality, were made using Pearson χ^2 tests for dichotomous outcomes and *t* tests or Kruskal–Wallis tests for continuous outcomes. Hierarchical 2-level logistic regression models with hospital identifier as a clustering effect were used to assess utilization of PCI in NSTEMI patients with CKD and in-hospital outcomes with covariates including age, sex, comorbidities, race, median household income, primary payer status, and hospital characteristics (weekend or weekday admission, hospital bed size, hospital region, and hospital teaching status). Comorbidities included in the regression models were obesity, hypertension, diabetes mellitus, heart

failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia. All analyses were weighted using NIS-provided weights to create national estimates.

To control for imbalances in patient characteristics and institutional characteristics between treatment groups, we constructed 4 separate match cohorts for all CKD subgroups. We used the same variables included in the above-mentioned hierarchical 2-level logistic regression models to predict likelihood (propensity) of receiving PCI (using separate multivariable logistic regression). Patients with the nearest propensity scores in 2 treatment groups (medical management only versus PCI) were matched using a 1:1 and 1:2 scheme without replacement using the Greedy method. Maximum propensity difference (caliper width) allowed was 0.05. Patients without matched observation were excluded. Simple logistic regression was used to generate odds ratios (ORs) for propensity score–matched cohorts. C index and Hosmer–Lemeshow goodness-of-fit tests were used to assess appropriateness of propensity score models.[18]

Outcomes

The primary outcome measured, in-hospital mortality, was assessed using hierarchical 2-level logistic regression and propensity score matching. Secondary outcomes assessed included rates of bleeding requiring transfusion, in-hospital death due to bleeding, and likelihood of undergoing PCI.

Results

Baseline Patient Characteristics

Of 4 488 795 patients hospitalized for NSTEMI, 1 373 118 (31%) underwent PCI (Table 1). Among all NSTEMI patients, 89% had no CKD (n=3 998 151), and 4.6% (n=207 351), 2.0% (n=88 179), and 4.3% (n=195 113) of NSTEMI patients had CKD stages 3, 4, and 5, respectively. Overall, 32% of NSTEMI patients with no CKD and 23%, 14%, and 22% with CKD stages 3, 4, and 5, respectively, underwent PCI. Figure 1 demonstrates adjusted all-cause, in-hospital mortality rates by treatment approach among NSTEMI patients with various stages of CKD severity, using propensity score–matched groups. In-hospital mortality was 1.2% among NSTEMI patients with no CKD who underwent PCI and 3.2% among those who did not undergo PCI ($P<0.001$). As CKD severity increased, in-hospital mortality increased among NSTEMI patients treated with revascularization and medical management. NSTEMI patients with CKD stage 5 who underwent PCI had in-hospital mortality of 3.9% compared with 9.0% if they did not undergo PCI ($P<0.001$).

Clinical and demographic differences as well as discharge characteristics in NSTEMI patients across CKD stages are shown in Tables 1 and 2. Prevalence of hypertension, diabetes mellitus, heart failure, and peripheral vascular disease significantly increased as CKD severity increased. As CKD stage increased, NSTEMI patients who underwent PCI were significantly more likely to be discharged to a facility as opposed to home, with 16% of NSTEMI patients with CKD stage 5 versus 5.3% of NSTEMI patients with no CKD being discharged to a facility after PCI. Furthermore, as CKD stage increased, NSTEMI patients who underwent PCI or medical management had significant greater cost of hospitalization and longer length of stay.

In-Hospital Outcomes Among NSTEMI Patients

Table 3 demonstrates the effect of CKD on all-cause, in-hospital mortality; rates of bleeding requiring transfusion; and all-cause, in-hospital death due to bleeding among NSTEMI patients after multivariate adjustment for age, sex, race, comorbidities, median household income, primary payer status, and hospital characteristics ($P<0.0001$). NSTEMI admission with severe CKD (stage $\geq$4) was associated with greater all-cause, in-hospital death compared with NSTEMI admission with no CKD; specifically, NSTEMI patients with CKD stage 5 had a 2.06 times higher likelihood of in-hospital death compared with NSTEMI patients with no CKD (OR: 2.06; 95% CI, 1.97–2.15; $P<0.0001$). NSTEMI patients admitted with CKD stage $\geq$3 had greater rates of bleeding requiring transfusion compared with those admitted with no CKD. NSTEMI patients admitted with CKD stage 5 had a 1.59 times higher likelihood of bleeding requiring transfusion compared with those admitted with no CKD (OR: 1.59; 95% CI, 1.48–1.71; $P<0.0001$). However, the impact of bleeding on in-hospital death was significant only among NSTEMI admissions with CKD stage 5 (OR: 1.97; 95% CI, 1.75–2.23; $P<0.0001$).

Management Characteristics

Table 4 demonstrates the adjusted likelihood of NSTEMI patients undergoing placement of a bare metal or drug-eluting stent. After multivariate logistic regression, NSTEMI patients with CKD stages 3, 4, and 5 had 10%, 41%, and 20% less likelihood, respectively, of undergoing PCI compared with NSTEMI patients with no CKD ($P<0.001$).

All-Cause, In-Hospital Mortality of NSTEMI Patients by Treatment Strategy

Table 5 illustrates the impact of CKD severity on all-cause, in-hospital mortality among NSTEMI patients who underwent medical management only or revascularization with PCI after multivariate logistic regression. NSTEMI patients with more

Table 1. Clinical and Demographic Characteristics of NSTEMI Admissions

	Overall			No CKD			CKD Stage 3			CKD Stage 4			CKD Stage 5/ESRD/Dialysis		
	N=4 488 795			n=3 998 151			n=207 351			n=88 179			n=195 113		
Characteristic	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value
Admissions, n	3 115 677	1 373 118		2 726 812	1 271 339		160 282	47 069		75 446	12 733		153 137	41 976	
Age, y, %			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001
18–34	0.7	0.7		0.8	0.7		0.2	0.1		0.2	0.2		0.8	0.8	
35–49	7	13		7.4	14		2.2	2.9		2.3	4.4		7.2	8.6	
50–64	24	37		25	38		14	19		14	18		30	36	
65–79	35	35		35	34		38	47		36	45		42	42	
≥80	33	15		33	14		46	31		48	32		20	12	
Sex, %			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001
Male	54	65		54	66		58	63		54	58		56	58	
Female	46	35		46	34		42	37		46	42		44	42	
Race, %			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001
White	63	64		64	65		68	68		65	65		45	46	
Black/Hispanic/ Asian	18	15		17	14		20	17		21	19		39	37	
Other	2.9	3.6		2.9	3.5		2.7	3.2		2.6	3		3.5	5.1	
Missing	16	17		16	18		10	12		12	13		13	12	
Comorbidities, %															
Obesity	11	14	<0.0001	11	14	<0.0001	16	20	<0.0001	13	17	<0.0001	10	13	<0.0001
Hypertension	69	71	<0.0001	68	70	<0.0001	83	87	<0.0001	78	83	<0.0001	86	90	<0.0001
Diabetes mellitus	39	35	<0.0001	36	33	<0.0001	53	57	<0.0001	57	62	<0.0001	62	68	<0.0001
Heart failure	41	20	<0.0001	38	17	<0.0001	62	47	<0.0001	70	59	<0.0001	59	52	<0.0001
Chronic pulmonary disease	25	18	<0.0001	25	17	<0.0001	28	25	<0.0001	27	25	<0.0001	22	21	<0.0001
Peripheral vascular disease	13	10	<0.0001	12	9.4	<0.0001	22	23	0.0305	22	26	<0.0001	23	24	0.0061
Smoking	16	27	<0.0001	17	28	<0.0001	9	12	<0.0001	7	8.8	<0.0001	8	8.9	<0.0001
Hyperlipidemia	50	67	<0.0001	50	67	<0.0001	59	72	<0.0001	53	63	<0.0001	42	53	<0.0001

CKD indicates chronic kidney disease; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention.

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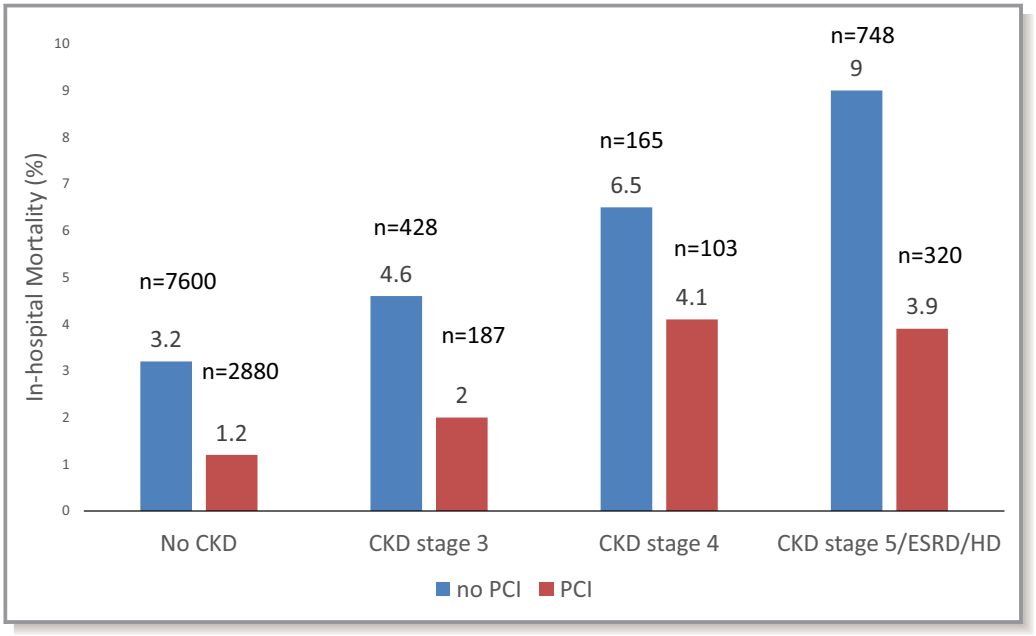

Figure 1. All-cause, in-hospital mortality of non–ST-segment–elevation myocardial infarction patients by CKD status in propensity score–matched groups. CKD indicates chronic kidney disease; ESRD, end-stage renal disease; HD, hemodialysis; PCI, percutaneous coronary intervention.

severe CKD had increased in-hospital mortality regardless of treatment approach compared with NSTEMI patients with no CKD. NSTEMI patients with CKD stage 5 who were medically managed had 2.04 times higher likelihood of in-hospital mortality compared with NSTEMI patients with no CKD (OR: 2.04; 95% CI, 1.95–2.13; $P<0.0001$). NSTEMI patients with CKD stage 5 who were treated with a bare metal or drug-eluting stent had 2.10 or 2.02 times higher likelihood, respectively, of in-hospital mortality compared with NSTEMI admissions with no CKD (base metal stent: OR: 2.10; 95% CI, 1.70–2.59; $P<0.001$; drug-eluting stent: OR 2.02; 95% CI 1.71–2.39, $P<0.001$).

All-Cause, In-Hospital Mortality in a Propensity Score–Matched Cohort

Table 6 demonstrates all-cause, in-hospital mortality in NSTEMI patients among different stages of CKD using propensity score–matched pairs (1:1) of PCI and medically treated patients. Among NSTEMI patients who underwent placement of a bare metal or drug-eluting stent, in-hospital mortality decreased in NSTEMI patients regardless of baseline level of CKD. Specifically, among NSTEMI patients with no CKD and with CKD stage 3, 4, or 5, PCI-treated groups had 63% ($P<0.0001$) and 57% ($P<0.0001$), 39% ($P<0.0001$), or 59% ($P<0.0001$) lower likelihood, respectively, of all-cause, in-hospital mortality compared with propensity score–matched medically managed groups.

To ensure proper balance between the propensity score–matched patients admitted for NSTEMI who did and did not undergo PCI, admission characteristics are provided for each CKD subgroup: no CKD (Table S1); CKD stage 3 (Table S2); CKD stage 4 (Table S3); and CKD stage 5, ESRD, or dialysis (Table S4). We noted no significant admission differences among the propensity score–matched groups in any CKD subgroup.

In addition, we performed ad hoc multivariate analysis to assess the interaction between PCI and CKD status on all-cause, in-hospital mortality (Table S5). We noted an interaction between PCI and CKD status. There was a declining reduction in mortality with PCI as CKD severity increased.

We also performed a propensity score match using a ratio of 1:2 (1 case to 2 controls). Using this method, we observed similar results regarding all-cause, in-hospital mortality in NSTEMI patients among different stages of CKD treated with PCI versus medical management (Table S6).

AKI Necessitating Hemodialysis

Figure 2 illustrates the incidence of AKI necessitating dialysis based on CKD stage using a propensity score–matched model. There was a significantly greater incidence of AKI requiring dialysis among NSTEMI patients admitted with CKD stage 4 who underwent PCI compared with the medically managed propensity score–matched group (7.28% versus 4.3%, $P<0.001$).

Table 2. Hospital and Discharge Characteristics of NSTEMI Admissions

	Overall			No CKD			CKD Stage 3			CKD Stage 4			CKD Stage 5/ESRD/Dialysis		
	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value	No PCI	PCI	*P* Value
			<0.0001			<0.0001			<0.0001			<0.0001			<0.0001
Discharge to home, %	58	92		58	93		58	84		58	78		55	79	
Discharge to facility, %	36	6.1		36	5.3		36	14		34	18		34	16	
In-hospital mortality, %	5.5	1.3	<0.0001	5.2	1.2	<0.0001	5.4	2.1	<0.0001	7.2	4.04	<0.0001	9.5	3.9	<0.0001
Median length of stay, d	4	3	<0.0001	4	3	<0.0001	5	4	<0.0001	5	6	<0.0001	5	5	<0.0001
Mean length of stay, d	5.6	3.7	<0.0001	5.4	3.5	<0.0001	6.4	5.6	<0.0001	6.8	7.7	<0.0001	7.9	6.7	<0.0001
Median cost of care ($)	10 168	19 309	<0.0001	9959	19 047	<0.0001	10 901	21 920	<0.0001	10 816	24 977	<0.0001	13 583	25 421	<0.0001
Mean cost of care ($)	17 478	22 751	<0.0001	17 087	22 243	<0.0001	18 402	26 454	<0.0001	16 915	30 348	<0.0001	23 847	31 803	<0.0001

CKD indicates chronic kidney disease; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention.

Discussion

Using the NIS database—the largest all-payer, inpatient-care database in the United States, representative of >95% of the population—we demonstrated the following results among NSTEMI patients from 2004 to 2014: (1) Increasing CKD severity was associated with increased rates of all-cause, in-hospital mortality and decreased utilization of PCI; (2) increasing CKD severity was associated with increasing bleeding requiring transfusion and in-hospital death due to bleeding; and (3) patients treated with PCI had less likelihood of all-cause, in-hospital mortality compared with propensity score–matched medically managed groups across all CKD subgroups.

Current reports anticipate that the United States will experience a considerable shift in its age structure, with the proportion of people aged >65 years expected to grow faster than any other age group and to increase by >60% in the next 15 years.[19] Furthermore, the incidence of acute myocardial infarction increases sharply with age. Whereas unstable angina, NSTEMI, and STEMI are often viewed as increasingly severe points along a disease spectrum, incidence rates of STEMI have declined significantly while NSTEMI rates have increased partly related to the aging population with multiple comorbidities.[20] Among the numerous risk factors for acute coronary syndrome, renal dysfunction has been found to be an independent risk factor for cardiovascular disease and is observed in 40% of patients with NSTEMI.[21,22]

There is a relative lack of representation of NSTEMI patients with advanced stages of CKD (stages 4 and 5) in large clinical trials. Observational studies have found that CKD is associated with poor in-hospital, short-term, and long-term outcomes among patients with NSTEMI.[23–25] In addition, some observational trials have shown that the outcomes of undergoing PCI are worse in patients with CKD compared with patients with normal renal function.[26–28] However, the benefit of early aggressive reperfusion therapy in CKD patients remains uncertain because these patients have traditionally been excluded from major clinical trials, with no dedicated RCTs of PCI versus medical therapy in this important subgroup. This situation is reflected in the current 2014 ACC/AHA and 2015 European Society of Cardiology guidelines, which state that there are “insufficient data on the benefit-to-risk ratio of an invasive strategy in patients with NSTEMI and advanced CKD (stages 4 and 5).” Well-matched retrospective analyses provide the most contemporary evidence for this population in the absence of RCTs.

Using propensity score matching to control for patient and hospital comorbidities, our results demonstrate the benefit of PCI regarding in-hospital mortality, even among NSTEMI patients with advanced CKD. Our findings expand those in the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease

Table 3. In-Hospital Outcomes of NSTEMI Admissions With Various CKD Stages

	In-Hospital Mortality		Bleeding Requiring Transfusion		In-Hospital Death Due to Bleeding	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
No CKD	Reference		Reference		Reference	
CKD stage 3	0.92 (0.87–0.97)	0.001	1.20 (1.12–1.30)	<0.001	0.89 (0.76–1.05)	0.170
CKD stage 4	1.13 (1.06–1.21)	<0.001	1.48 (1.35–1.63)	<0.001	1.05 (0.86–1.30)	0.629
CKD stage 5/ESRD/dialysis	2.06 (1.97–2.15)	<0.001	1.59 (1.48–1.71)	<0.001	1.97 (1.75–2.23)	<0.001

Multivariable logistic regression adjusted for age, sex, race, mode of therapy (medical management, placement of bare metal stent, or placement of drug-eluting stent), comorbidities (obesity, hypertension, diabetes mellitus, heart failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia), median household income, primary payer insurance status, admission type (elective vs non elective), admission day (weekend or weekday), hospital bed size, hospital region, and hospital teaching status. CI indicates confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; OR, odds ratio.

Evaluated According to Recommended Therapies) study, which revealed that an early invasive strategy was associated with improved short-term survival in NSTEMI patients with mild–moderate renal insufficiency. However, this benefit declined with lower renal function and was not clear in those with renal failure or who were on dialysis.[9] Previous subgroup analysis of 5 RCTs, called VINO (Value of First Day Coronary Angiography/Angioplasty In Evolving Non ST-Segment Elevation Myocardial Infarction), FRISC II (The Framingham and Fast Revascularization During Instability in Coronary Artery Disease), TIMI IIIB (Thrombolysis in myocardial infarction IIIB clinical trial), ICTUS (Invasive vs Conservative Treatment in Unstable Coronary Syndromes), and TACTICS-TIMI 18 (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18), TIMI IIIB (Thrombolysis in myocardial infarction IIIB clinical trial), ICTUS (Invasive vs Conservative Treatment in Unstable Coronary Syndromes), and TACTICS-TIMI 18 (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18), compared the outcomes of an early invasive versus conservative approach in patients presenting with NSTEMI. Of the 7481 randomly assigned patients, only 267 patients had CKD stage 4 or 5, and the majority of patients

Table 4. Likelihood of Undergoing PCI Among NSTEMI Admissions With Various CKD Stages

	PCI		BMS		DES	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
No CKD	Reference		Reference		Reference	
CKD stage 3	0.90 (0.86–0.93)	<0.001	0.97 (0.92–1.03)	0.3635	0.86 (0.83–0.90)	<0.001
CKD stage 4	0.59 (0.56–0.62)	<0.001	0.64 (0.59–0.70)	<0.001	0.57 (0.53–0.60)	<0.001
CKD stage 5/ESRD/dialysis	0.80 (0.78–0.83)	<0.001	0.87 (0.82–0.91)	<0.001	0.78 (0.75–0.81)	<0.001

Multivariable logistic regression adjusted for age, sex, race, comorbidities (obesity, hypertension, diabetes mellitus, heart failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia), median household income, primary payer insurance status, admission type (elective vs non elective), admission day (weekend or weekday), hospital bed size, hospital region, and hospital teaching status. BMS indicates bare metal stent; CI, confidence interval; CKD, chronic kidney disease; DES, drug-eluting stent; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention.

Table 5. All-Cause, In-Hospital Mortality of NSTEMI Admissions With Various CKD Stages

	Medical Management		BMS		DES	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
No CKD	Reference		Reference		Reference	
CKD stage 3	0.91 (0.86–0.96)	<0.001	1.07 (0.85–1.35)	0.590	0.92 (0.74–1.13)	0.432
CKD stage 4	1.10 (1.03–1.18)	0.008	1.45 (1.00–2.09)	0.050	1.73 (1.34–2.23)	<0.001
CKD stage 5/ESRD/dialysis	2.04 (1.95–2.13)	<0.001	2.10 (1.70–2.59)	<0.001	2.02 (1.71–2.39)	<0.001

Multivariable logistic regression adjusted for age, sex, race, comorbidities (obesity, hypertension, diabetes mellitus, heart failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia), median household income, primary payer insurance status, admission type (elective vs non elective), admission day (weekend or weekday), hospital bed size, hospital region, and hospital teaching status. BMS indicates bare metal stent; CI, confidence interval; CKD, chronic kidney disease; DES, drug-eluting stent; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; OR, odds ratio.

Table 6. Impact of PCI on All-Cause, In-Hospital Mortality Among NSTEMI Admissions

CKD Stage	Matched Pairs, n	Medical Management	PCI		
			OR (95% CI)	*P* Value	AUC
No CKD	232 786	Reference	0.37 (0.36–0.39)	<0.001	0.72
CKD stage 3	9355	Reference	0.43 (0.36–0.51)	<0.001	0.67
CKD stage 4	2525	Reference	0.61 (0.48–0.79)	<0.001	0.66
CKD stage 5/ESRD/dialysis	8300	Reference	0.41 (0.36–0.47)	<0.001	0.64

Propensity model adjusted for age, sex, race, comorbidities (obesity, hypertension, diabetes mellitus, heart failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia), median household income, primary payer insurance status, admission type (elective vs non elective), admission day (weekend or weekday), hospital bed size, hospital region, and hospital teaching status. AUC indicates area under the curve; CI, confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; NSTEMI, non–ST-segment–elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention.

were from the TIMI IIIB trial, the oldest trial included in the pooled analysis.[29] The study revealed that an early invasive strategy was associated with significant reduction in rehospitalizations but nonsignificant reduction in all-cause mortality. It is possible that pooled analysis of the VINO, FRISC II, ICTUS, TIMI IIIB, and TACTICS-TIMI 18 studies was underpowered to detect significant reductions in mortality in NSTEMI patients with advanced stages of CKD undergoing PCI. This is exemplified by the fact that a relatively small number of trials were included in the pooled analysis, with only a modest number of patients with CKD stage ≥3 and a low number of fatalities. Furthermore, heterogeneity of the trials that were included in this pooled analysis also may have contributed to the lack of statistically significant benefit.

Previous studies have also demonstrated baseline renal function is a strong independent predictor of in-hospital mortality after NSTEMI treated with early revascularization.[30–32] Our study results expand on these findings because we found that baseline renal function is not only a significant independent predictor of in-hospital death among patients who underwent revascularization but also a significant independent predictor of in-hospital mortality among NSTEMI patients who underwent medical management only. Adjusted analysis showed that NSTEMI patients with CKD stage 5, ESRD, or dialysis who underwent medical management had significantly higher in-hospital mortality only compared with those with no CKD. This finding may be partially explained by the greater comorbidity burden we noted as renal function worsened among NSTEMI patients. NSTEMI patients with severe renal impairment are less likely to be given standard medical therapy including aspirin, beta blockers, and angiotensin-converting enzyme inhibitors, even among those considered "ideal" candidates.[33] Recent data from the ACTION registry demonstrated lower use of evidence-based therapies, in-hospital procedures, and cardioprotective medications as well as frequent overdosing of medications among NSTEMI patients with severe CKD.[22] Our findings are in line with these results: We found that increasing CKD severity was associated with significantly decreased utilization of bare metal or drug-eluting stents and increased bleeding risk. Patients with CKD stages 4 and 5 had the lowest utilization of PCI for NSTEMI treatment. This may be partially explained by fear of increased risk of contrast-induced nephropathy transitioning to dialysis.[25,34–36] Using propensity score–matched NSTEMI admissions, our results demonstrated that the incidence of AKI requiring hemodialysis was significantly higher among NSTEMI patients admitted with CKD stage 4 who underwent PCI compared with those who did not; however, our study database did not allow us to define the timing of AKI relative to when PCI was performed.

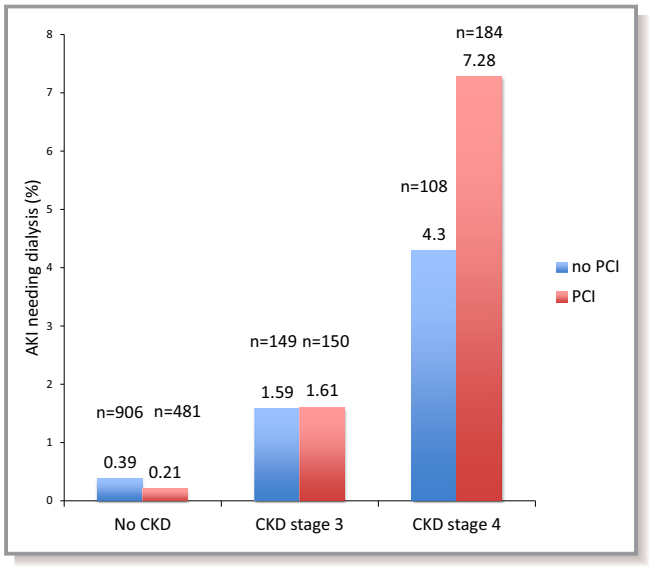

Figure 2. AKI needing dialysis based on CKD stage. AKI indicates acute kidney injury; CKD, chronic kidney disease; PCI, percutaneous coronary intervention.

Shroff et al have shown that among patients presenting with acute coronary syndrome, the likelihood of in-hospital bleeding and mortality for patients with advanced CKD was 62% and 44% higher, respectively, compared with non-CKD patients ($P<0.001$).[37] Advanced CKD was defined as creatinine ≥2.5 mg/dL. Similarly, our study found the likelihood of bleeding requiring transfusion was 20%, 48%, and 59% higher

among NSTEMI patients with CKD stages 3, 4, and 5 (or with ESRD or on hemodialysis or peritoneal dialysis), respectively, compared with patients with no CKD. However, we found that in-hospital death due to bleeding was significantly greater only among NSTEMI patients with CKD stage 5, ESRD, or hemodialysis; these patients had 1.97 times greater in-hospital mortality compared with those with no CKD. Differences in our results may be partially explained by differences in patient groups—Shroff et al identified acute coronary syndrome patients according to advanced CKD, non-CKD, and use of dialysis.

Our study must be interpreted in light of its limitations. We could not account for the various factors that influence the decision to manage a patient medically versus invasively, specifically, individual patient preference, cardiovascular risk, and comorbidities. Consequently, no causal relationship could be determined between in-hospital outcomes and medical management or PCI. Furthermore, there is likely selection bias in terms of which patients received PCI versus medical management, and that bias could not be accounted for using this database. Because of the constraints of the database, we could not identify patients who underwent angiography and then underwent surgical intervention. In addition, there is a possibility of coding errors, although we do not suspect these errors to affect certain study subgroups more than others. We were also unable to obtain information regarding the amount of contrast used or the rates of contrast nephropathy in patients who underwent PCI, and we did not have information on the types of medications used in patients who did or did not undergo PCI. We also did not have detailed clinical and laboratory data to detect the presence of kidney damage, such as degree of albuminuria, urinary sediment abnormalities, and pathologic histological abnormalities. Moreover, propensity score matching may not have made the groups alike regarding important unmeasured confounders.

There is a high likelihood of differential misclassification in our study. Previous research has shown that clinicians are more likely to code for severe CKD than mild CKD, especially given the high prevalence of multicomorbidity among CKD patients.[15] Consequently, there is limited sensitivity of *ICD-9-CM* coding for mild CKD. To mitigate this misclassification, we did not include NSTEMI patients with CKD stages 1 and 2; however, there is still a high possibility of this effect among our study groups. Although speculative, this approach may have resulted in less prevalence and accuracy of in-hospital outcomes among NSTEMI patients with CKD stages 3 and 4 compared with NSTEMI patients with CKD stage 5 or ESRD.

Conclusion

Using the largest publicly available, in-hospital database in the United States, our results indicate that use of PCI decreases among NSTEMI patients as CKD severity increases and that all-cause, in-hospital mortality is greater in NSTEMI patients with more severe CKD regardless of treatment strategy. Patients with CKD presenting with NSTEMI appear to benefit from PCI compared with medical therapy. Prospective studies and RCTs are warranted to substantiate these findings and to assess the best revascularization strategies for this highly vulnerable population.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Propensity demographics for NSTEMI admissions with no CKD.

	No PCI	PCI	P-value
Total number of admissions	232,786	232,786	
Mean age (years)	65	65	0.459
Sex(%)			0.498
Male	64	63	
Female	36	37	
Race (%)			0.674
White	65	65	
Black/Hispanic/Asian	15	15	
Other	3.2	3.3	
Missing	17	17	
Comorbidities (%)			
Obesity	14	14	0.6455
Hypertension	70	71	0.875
Diabetes	34	33	0.221
Heart failure	18	18	0.5863
Chronic pulmonary disease	18	18	0.522
Peripheral vascular disease	10	9.8	0.48
Smoking	25	26	<0.001
Hyperlipidemia	65	65	0.4595
Median household income (%)			0.456
1. 0-25th percentile	28	28	
2. 26-50th percentile	28	27	
3. 51-75th percentile	24	24	
4. 76-100th percentile	20	21	
Primary Payer (%)			0.158

Medicare / Medicaid	58	56	
Private, including HMO	32	33	
Self pay/no charge/other	9.9	10	
Admission type (%)			0.317
Non elective	91	91	
elective	8.6	8.9	
Admission day (%)			0.1534
Weekday	76	76	
Weekend	24	24	
Hospital bed size (%)			0.427
Small	7.6	7.9	
Medium	22	22	
Large	70	70	
Hospital region (%)			0.064
Northeast	18	18	
Midwest	24	24	
South	42	41	
West	17	17	
Hospital teaching status (%)			0.164
Non teaching	46	45	
Teaching	54	55	

Table S2. Propensity demographics for NSTEMI admissions with CKD stage 3 .

	No PCI	PCI	P-value
Total number of admissions	9355	9355	
Mean age (years)	73	73	0.614
Sex(%)			0.421
Male	63	63	
Female	37	37	

Race (%)			0.587
White	68	68	
Black/Hispanic/Asian	17	17	
Other	3.4	3.1	
Missing	11	12	
Comorbidities (%)			
Obesity	20	20	0.828
Hypertension	87	87	0.555
Diabetes	57	57	0.660
Heart failure	48	47	0.198
Chronic pulmonary disease	26	25	0.368
Peripheral vascular disease	23	23	0.668
Smoking	12	12	0.423
Hyperlipidemia	72	72	0.612
Median household income (%)			0.660
1. 0-25th percentile	29	29	
2. 26-50th percentile	29	29	
3. 51-75th percentile	23	24	
4. 76-100th percentile	19	19	
Primary Payer (%)			0.171
Medicare / Medicaid	82	81	
Private, including HMO	14	15	
Self pay/no charge/other	3.8	3.9	
Admission type (%)			0.328
Non elective	93	93	
elective	6.8	7.1	
Admission day (%)			0.594
Weekday	77	76	
Weekend	23	24	
Hospital bed size (%)			0.210
Small	8.7	9.2	

Medium	21	21	
Large	71	70	
Hospital region (%)			0.324
Northeast	14	15	
Midwest	30	31	
South	39	38	
West	17	17	
Hospital teaching status (%)			0.701
Non teaching	42	42	
Teaching	58	58	

Table S3. Propensity demographics for NSTEMI admissions with CKD stage 4.

	No PCI	PCI	P-value
Total number of admissions	2525	2525	
Mean age (years)	73	72	
Sex (%)			0.405
Male	59	58	
Female	41	42	
Race (%)			0.984
White	64	64	
Black/Hispanic/Asian	19	19	
Other	2.9	2.9	
Missing	13	14	
Comorbidities (%)			
Obesity	17	18	0.532
Hypertension	83	83	0.906
Diabetes	64	62	0.189
Heart failure	60	59	0.423
Chronic pulmonary disease	25	25	0.961
Peripheral vascular disease	25	26	0.684

Smoking	8.3	8.8	0.584
Hyperlipidemia	63	63	0.928
Median household income (%)			0.968
1. 0-25th percentile	29	30	
2. 26-50th percentile	29	29	
3. 51-75th percentile	24	23	
4. 76-100th percentile	18	18	
Primary Payer (%)			0.571
Medicare / Medicaid	83	83	
Private, including HMO	13	14	
Self pay/no charge/other	3.8	3.4	
Admission type (%)			0.466
Non elective	93	92	
elective	7.3	7.8	
Admission day (%)			0.629
Weekday	76	76	
Weekend	24	24	
Hospital bed size (%)			0.686
Small	8.2	8.7	
Medium	23	22	
Large	69	69	
Hospital region (%)			0.938
Northeast	15	16	
Midwest	30	29	
South	40	40	
West	15	15	
Hospital teaching status (%)			0.755
Non teaching	40	41	
Teaching	60	59	

Table S4. Propensity demographics for NSTEMI admissions with CKD stage 5 .			
	No PCI	PCI	P-value
Total number of admissions	8300	8300	
Mean age (years)	65	65	0.306
Sex(%)			0.9717
Male	58	58	
Female	42	42	
Race (%)			0.7035
White	46	46	
Black/Hispanic/Asian	38	37	
Other	4.6	4.9	
Missing	11	12	
Comorbidities (%)			
Obesity	13	13	0.8538
Hypertension	91	90	0.1163
Diabetes	68	68	0.4964
Heart failure	52	52	0.9192
Chronic pulmonary disease	21	21	0.2262
Peripheral vascular disease	24	24	0.846
Smoking	8.7	9	0.478
Hyperlipidemia	53	53	0.906
Median household income (%)			0.624
1. 0-25th percentile	35	34	
2. 26-50th percentile	25	25	
3. 51-75th percentile	23	23	
4. 76-100th percentile	17	18	
Primary Payer (%)			0.9822
Medicare / Medicaid	86	86	
Private, including HMO	12	12	
Self pay/no charge/other	2.2	2.3	
Admission type (%)			0.0321

Non elective	92	91	
elective	8	8.9	
Admission day (%)			0.3169
Weekday	79	79	
Weekend	21	21	
Hospital bed size			0.4593
Small	5.9	6.3	
Medium	21	22	
Large	73	72	
Hospital region (%)			0.384
Northeast	18	18	
Midwest	20	21	
South	40	39	
West	22	22	
Hospital teaching status (%)			0.5394
Non teaching	39	38	
Teaching	61	62	

Table S5. Multivariate analysis to assess interaction between CKD and PCI on all-cause in-hospital mortality.

	Odds ratio (95% CI)	P-value
No CKD & PCI	0.34 (0.32-0.35)	<0.001
CKD stage 3 & PCI	0.40 (0.35-0.47)	<0.001
CKD stage 4 & PCI	0.72 (0.59-0.88)	0.001
CKD stage 5/ESRD/Dialysis & PCI	0.84 (0.75-0.94)	0.002

CKD = chronic kidney disease; ESRD = end-stage renal disease; CI = confidence interval; PCI = percutaneous coronary intervention

Table S6. Impact of PCI on all-cause in hospital mortality on NSTEMI admissions.

CKD stage	Number of matched pairs	Medical Management	PCI	
			Odds ratio (95% CI)	P-value
No CKD	122,057	*Reference*	0.41 (0.39-0.43)	<0.001
Stage 3	8,277	*Reference*	0.45 (0.38-0.53)	<0.001
Stage 4	2,498	*Reference*	0.65 (0.52-0.81)	0.002
Stage 5, ESRD, or on HD	7,997	*Reference*	0.43 (0.38-0.48)	<0.001

Propensity score match (1:2) model adjusted for age, sex, race, comorbidities (obesity, hypertension, diabetes, heart failure, chronic pulmonary disease, peripheral vascular disease, smoking, and hyperlipidemia), median household income, primary payer insurance status, admission type (elective vs non elective), admission day (weekend or weekday), hospital bed size, hospital region, and hospital teaching status.

Non–ST–Segment–Elevation Myocardial Infarction Among Patients With Chronic Kidney Disease: A Propensity Score–Matched Comparison of Percutaneous Coronary Intervention Versus Conservative Management

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