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Acute Kidney Injury After CABG Versus PCI



An Observational Study Using 2 Cohorts

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ABSTRACT

BACKGROUND Acute kidney injury (AKI) is a known complication after coronary revascularization, but few studies have directly compared the incidence of AKI after coronary artery bypass surgery (CABG) or after percutaneous coronary intervention (PCI) in similar patients.

OBJECTIVES The aim of this study was to investigate whether multivessel CABG compared with PCI as an initial revascularization strategy is associated with a higher risk for AKI.

METHODS A retrospective analysis of patients undergoing first documented coronary revascularization was conducted using 2 complementary cohorts: 1) Kaiser Permanente Northern California, a diverse, integrated health care delivery system; and 2) Medicare beneficiaries, a large, nationally representative older cohort. AKI was defined in the Kaiser Permanente Northern California cohort by an increase in serum creatinine of \geq 0.3 mg/dl or \geq 150% above baseline and in the Medicare cohort by discharge diagnosis codes and the use of dialysis.

RESULTS The incidence of AKI was 20.4% in the Kaiser Permanente Northern California cohort and 6.2% in the Medicare cohort. The incidence of AKI requiring dialysis was <1%. CABG was associated with a 2- to 3-fold significantly higher adjusted odds for developing AKI compared with PCI in both cohorts.

CONCLUSIONS AKI is common after multivessel coronary revascularization and is more likely after CABG than after PCI. The risk for AKI should be considered when choosing a coronary revascularization strategy, and ways to prevent AKI after coronary revascularization are needed. (J Am Coll Cardiol 2014;64:985-94) © 2014 by the American College of Cardiology Foundation.

cute kidney injury (AKI) is a well-known complication after surgical or percutaneous coronary revascularization, ranging in prevalence between 1% and 30% depending on the study population and the definition of AKI (1-5). Patients who develop AKI not only have longer hospital stays and higher incidence of other periprocedural complications but also have a higher risk for long-term adverse outcomes, including chronic kidney disease (CKD), end-stage renal disease, and death (6-11).

Although there are shared risk factors for AKI after coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), such as older age or pre-existing CKD, there are also factors unique to each type of revascularization (5,11,12). For example, the use of cardiopulmonary bypass is associated with post-CABG AKI, while PCI can lead to AKI from contrast-induced nephropathy. Although numerous publications have evaluated AKI in the setting of either CABG or PCI, few have directly compared CABG with PCI on the risk for AKI in similar patients.

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ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

CABG = coronary artery bypass grafting

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

KPNC = Kaiser Permanente Northern California

PCI = percutaneous coronary intervention Therefore, a better understanding of the relative risk for AKI after CABG compared with PCI is needed to inform patients and promote shared decision making.

SEE PAGE 995

Toward that end, we examined whether isolated multivessel CABG compared with multivessel PCI as an initial coronary revascularization strategy would be associated with a higher risk for AKI in 2 complementary populations: Kaiser Permanente Northern California (KPNC), a large, integrated health care delivery system with detailed inpatient and outpatient laboratory and other clinical information, and Medicare beneficiaries, a large cohort with administrative claims data that are representative of the older population in the United States.

METHODS

COHORT ASSEMBLY: KPNC. KPNC cares for more than 3.3 million persons who are representative of the local and statewide population, apart from slightly lower representation of the extremes of age and income (13). To construct a cohort of patients with isolated CABG or PCI as the initial revascularization strategy for multivessel coronary disease, we identified all health plan members \geq 30 years of age who underwent multivessel (≥2-vessel) CABG or PCI procedures between January 1, 1996, and December 31, 2008, by International Classification of Diseases-Ninth Edition, codes 36.0, 36.00, 36.01, 36.02, 36.05, 36.06, 36.07, 36.09, 36.10, 36.11, 36.12, 36.13, 36.14, 36.15, 36.16, 36.17, and 36.19 and Current Procedure Terminology, Fourth Edition, codes 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536, 33572, 92973, 92980, 92981, 92982, 92984, 92995, and 92996. To capture complete data, we restricted the analysis to patients with complete demographic data and at least 12 months of continuous membership and pharmacy benefit before the index revascularization procedure (Figure 1). Using logistic regression with receipt of CABG or PCI as the outcome, we calculated a propensity score (14) for each patient using baseline sociodemographic and clinical characteristics (Online Table 1). We matched each patient who underwent multivessel PCI with up to 3 patients (15) who underwent multivessel CABG using a greedy matching algorithm that matched propensity scores to a maximum caliper width of 0.01 (16). We additionally required that patients be matched exactly on year of the index procedure.

COHORT ASSEMBLY: MEDICARE. The Medicare study population consisted of fee-for-service Medicare beneficiaries who underwent multivessel CABG or multivessel PCI between 1992 and 2008. To permit a 1-year retrospective evaluation period and to document the presence of comorbid conditions, we restricted the study sample to patients 66 years of age or older with both Medicare Part A and Part B coverage. We identified hospitalizations for coronary revascularization from 20% Part A data and identified patients by International Classification of Diseases-Ninth Revision, procedure codes and Current Procedural Terminology-Fourth Edition, codes using methods analogous to the construction of the KPNC cohort (Figure 2). Using logistic regression with receipt of CABG or PCI as the outcome, we calculated a propensity score (14) for each patient using baseline demographic and comorbid characteristics (Online Table 2). Given the large sample size, we matched each patient who underwent multivessel PCI with 1 patient who underwent multivessel CABG using a greedy matching algorithm that first matched propensity scores at 7 digits, then at 6 digits, and so forth, down to a minimum 2-digit match (17). We additionally required that patients be matched on year of the index procedure, diabetes status, and age within 1 year (Figure 2).

In both the KPNC and Medicare cohorts, we excluded patients who had single-vessel PCI or CABG, patients in whom the number of vessels revascularized was unknown, and patients undergoing concomitant cardiac procedures at the time of CABG. We excluded patients with any prior coronary revascularization, a history of organ transplantation, and patients with a history of maintenance dialysis.

BASELINE KIDNEY FUNCTION. In the KPNC cohort, baseline serum creatinine level was defined as the most recent outpatient, non-emergency department serum creatinine level measured with an isotope dilution mass spectrometry-traceable assay (18) between 7 and 365 days before the index date. For nonurgent revascularization procedures, we also allowed the use of a serum creatinine level measured on the index date (19). We calculated the estimated glomerular filtration rate (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration equation (20) and categorized patients into the following 3 groups: ≥60, 45 to 59, and <45 ml/min/1.73 m². We defined patients with pre-existing CKD as having eGFRs <60 ml/min/1.73 m².

In the Medicare cohort, we identified the presence or absence of baseline CKD using a previously validated claims-based algorithm (21). This algorithm has relatively low sensitivity (26%) but high specificity (93.4%) for identifying CKD in Medicare claims data.

OUTCOMES: AKI. In the KPNC cohort, we defined the outcome on the basis of the maximum serum creatinine level measured during the index hospitalization but after the revascularization procedure. We defined AKI stages 1, 2, and 3 on the basis of modified Acute Kidney Injury Network criteria (22): 1) a relative increase in serum creatinine of ≥150% to 200% above baseline or an absolute increase in serum creatinine of \geq 0.3 mg/dl above baseline; 2) a relative increase in serum creatinine to more than 200% to 300% above baseline; or 3) a relative increase in serum creatinine to >300% above baseline or a \geq 4.0 mg/dl absolute increase with an acute increase of at least 0.5 mg/dl, or the use of renal replacement therapy. Because only 2 patients had stage 2 AKI and 35 patients had stage 3 AKI, we grouped all stages of AKI together. We also conducted a sensitivity analysis, defining AKI as an absolute increase in serum creatinine of 0.5 mg/dl above baseline, a definition that has been used in several previous studies of AKI (23). We excluded patients without inpatient serum creatinine measurements and patients who developed AKI during the index hospitalization but before the revascularization procedure (Figure 1).

In the Medicare cohort, we defined AKI using any diagnosis code for 584.x during the index hospitalization and AKI requiring dialysis as a diagnosis code for AKI plus a dialysis procedure code (V39.95, V45.1, V56.0, or V56.1) (24). We also examined whether patients who were discharged alive from the index hospitalization required dialysis 90 days after the index date as a measure of chronic dialysis, defined as the presence of a dialysis procedure code on day 89, 90, or 91 (because outpatient hemodialysis is usually performed thrice weekly on Monday, Wednesday, and Friday or Tuesday, Thursday, and Saturday).

COVARIATES. In the KPNC cohort, we identified age, sex, self-reported race/ethnicity, and comorbid conditions up to 4 years before the index date and throughout the duration of follow-up, by using previously validated approaches based on International Classification of Diseases-Ninth Revision, diagnosis and procedure codes and Current Procedural Terminology-Fourth Edition, procedure codes identified from health plan hospitalization, ambulatory, laboratory, and pharmacy databases (25-31). Information



grafting (CABG) and 1,004 patients who underwent multivessel percutaneous coronary intervention (PCI). AKI = acute kidney injury; KPNC = Kaiser Permanente Northern California.

on the conditions is listed in **Table 1**. We also collected selected laboratory test results up to 1 year before or on the index date. We ascertained baseline use of the following medications on the basis of information from pharmacy records using previously validated methods (32,33): angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretic agents, beta-blockers, calcium-channel blockers, nitrates, hydralazine, alpha-adrenergic antagonists, aldosterone receptor antagonists, digoxin, statins, nonstatin lipid-lowering agents, aspirin, antiplatelet agents, anti-inflammatory agents, and diabetes medications.

In the Medicare cohort, we defined comorbidities using Part A and Part B data (composed of a 5%



random sample from 1992 to 1997 and a 20% random sample from 1998 to 2008). We defined comorbid conditions using outpatient and inpatient encounters in the year before the index procedure and considered a comorbidity to be present if it was recorded as a primary or secondary diagnosis code on an inpatient admission or outpatient encounter. The characteristics are listed in Table 2.

STATISTICAL ANALYSIS. All analyses were conducted separately for the KPNC and Medicare cohorts. Differences between patients undergoing CABG and those undergoing PCI were compared using standardized differences. Standardized differences are an alternative to p values to describe differences between groups and are not influenced by sample size. Standardized differences >10% represent meaningful imbalance between groups (34).

For both cohorts, we calculated the odds ratio and 95% confidence interval associated with CABG compared with PCI on AKI in the propensity scorematched cohort without additional adjustment for specific covariates. We hypothesized that the association of AKI with revascularization type would be modified by baseline CKD status or diabetes mellitus status. To address this in the KPNC cohort, we conducted separate stratified analyses on the basis of baseline eGFR (\geq 60, 45 to 59, or <45 ml/min/1.73 m²) and baseline diabetes mellitus status. In the Medicare cohort, we fitted models with a multiplicative interaction term (additive on the log scale) for the presence or absence of CKD and separately for the presence or absence of diabetes mellitus, and we report model estimates for those patients with and without these factors.

We also conducted another sensitivity analysis using the methods proposed by Lin et al. (35), to assess whether an unmeasured confounder could account for the observed differences in the odds of AKI among patients undergoing CABG versus PCI.

The institutional review boards of the Kaiser Foundation Research Institute and Stanford University approved the study. A waiver of the requirement for informed consent was obtained because of the nature of the study. All analyses were performed using SAS versions 9.1.3 and 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

In the KPNC cohort, predictors of undergoing CABG compared with PCI included calendar year, male sex, and a history of unstable angina (Online Table 1). The KPNC propensity score model had a cstatistic of 0.856 (Online Figure 1). Of the patients undergoing PCI, 36.5% were matched with 3 patients undergoing CABG, 19.6% were matched with 2 patients undergoing CABG, and 43.9% were matched with 1 patient undergoing CABG. Overall, we matched 82% of the patients who had multivessel PCI (1,004 of 1,222) to 1,933 patients undergoing multivessel CABG in the KPNC cohort. In the Medicare cohort, predictors of undergoing CABG rather than PCI were calendar year, age, sex, and diabetes (Online Table 2). The Medicare propensity score model had a c-statistic of 0.673 (Online Figure 2). We matched 19.2% of patients on 5 to 7 digits of propensity score, 31.7% on 4 digits, 39.5% on 3 digits, and 9.6% on 2 digits. Overall, 92% of patients who underwent multivessel PCI were matched with patients who underwent multivessel CABG in the Medicare cohort. Baseline characteristics in both propensity score-matched cohorts were well balanced among patients undergoing multivessel PCI and multivessel CABG (Tables 1 and 2).

During the index hospitalization, 20.4% of patients in the KPNC cohort and 6.2% of patients in the Medicare cohort developed AKI on the basis of

TABLE 1 Baseline Clinical Characteristics of the Matched KPNC
Cohort of Adults Age 30 Years or Older Undergoing Multivessel
Coronary Revascularization

Variable	CABG (n = 1,933)	PCI (n = 1,004)	Standardized Difference
Demographics			
Age, yrs			
<65	39.9	39.6	0.6
65-74	33.2	30.9	4.9
≥75	26.9	29.5	5.8
Women	26.9	30.5	8.0
Race			
White	74.9	75.2	0.7
Black/African American	3.9	4.8	4.4
Asian/Pacific Islander	13.4	12.5	2.7
Other	7.9	7.6	1.1
Hispanic ethnicity	13.9	13.1	2.3
Cardiovascular history			
Prior myocardial infarction	33.4	36.9	7.3
Unstable angina	24.0	22.3	4.0
Heart failure	9.0	9.3	1.0
Cerebrovascular disease	16.7	16.4	0.8
Stroke or transient ischemic attack	3.7	3.7	0.0
Peripheral arterial disease	3.8	3.8	0.0
Mitral/aortic valve disease	6.4	6.6	0.8
Atrial fibrillation/flutter	9.3	9.5	0.7
Ventricular fibrillation/ tachycardia	1.2	1.4	1.8
Other medical history			
Diabetes mellitus	39.2	38.0	2.5
Hypertension	68.0	68.2	0.4
Dyslipidemia	85.2	85.2	0.0
Chronic lung disease	18.4	18.3	0.3
Chronic liver disease	1.5	1.6	0.8
Diagnosed depression	13.7	14.7	2.9
Dementia	0.9	1.4	4.7
Hyperthyroidism	0.7	0.7	0.0
Hypothyroidism	11.3	12.3	3.1
Systemic cancer	11.2	11.4	0.6
Hospitalized bleed	2.3	2.2	0.7
Laboratory values			
Hemoglobin, g/l eGFR, ml/min/1.73 m ²	13.9 ± 1.6	13.9 ± 1.7	0.0
≥60	56.0	54.4	3.2
45-59	26.9	26.9	0.0
<45 (not on dialysis)	17.1	18.7	4.2

Continued in the next column

cohort-specific criteria. More CABG patients than PCI patients developed AKI, and more patients with baseline CKD developed AKI (Figure 3, Central Illustration). In the KPNC cohort, CABG was consistently associated with 1.6 higher odds of AKI compared with PCI overall and 1.3- to 2.0-fold higher odds in models stratified by baseline eGFR (Table 3). The confidence intervals overlapped the point estimates across eGFR and diabetes mellitus strata,

TABLE 1 Continued			
Variable	CABG (n = 1,933)	PCI (n = 1,004)	Standardized Difference
Baseline medication use			
Angiotensin-converting enzyme inhibitors	41.1	40.0	2.2
Angiotensin II receptor blockers	8.9	9.2	1.0
Diuretic agents	40.5	41.7	2.4
Beta-blockers	58.4	56.4	4.0
Calcium-channel blockers	25.3	24.8	1.2
Nitrates	23.6	21.3	5.5
Hydralazine	2.6	3.6	5.8
Alpha-adrenergic receptor antagonists	13.6	13.3	0.9
Aldosterone antagonists	1.2	1.2	0.0
Digoxin	6.1	6.0	0.4
Statins	55.5	54.3	2.4
Nonstatin lipid-lowering agents	5.2	4.6	2.8
Aspirin	7.1	6.9	0.8
Antiplatelet agents	5.5	5.1	1.8
Anti-inflammatory agents	18.2	18.7	1.3
Diabetes medications	30.5	29.4	2.4

Values are % or mean \pm SD.

CABG = coronary artery bypass grafting; eGFR = estimated glomerular filtration rate; KPNC = Kaiser Permanente Northern California; PCI = percutaneous coronary intervention.

indicating no clinically relevant effect modification by these variables in the KPNC cohort. Results were not materially changed in sensitivity analyses in which AKI was defined as an absolute increase in serum creatinine of ≥ 0.5 mg/dl higher than baseline (Online Table 3). In the Medicare cohort, CABG was associated with 2.6-fold higher odds of AKI compared with PCI (Table 3). The magnitude of the association was smaller for patients with baseline CKD and diabetes mellitus than for patients without these comorbid conditions.

The incidence of AKI requiring dialysis during the index hospitalization was low in both cohorts: 0.4% (n = 12) in KPNC and 0.2% (n = 252) in Medicare. The low incidence of AKI requiring dialysis in the KPNC cohort precluded further analysis of this outcome. In the Medicare cohort, the incidence of AKI requiring dialysis was higher in patients undergoing CABG (0.4%) versus PCI (0.1%) (p < 0.0001; odds ratio: 2.66; 95% confidence interval: 2.01 to 3.51) overall and in the subset of patients with CKD: 2.9% of CABG and 1.3% of PCI patients (p < 0.0001; odds ratio: 2.3; 95% confidence interval: 1.4 to 3.8).

A significant proportion of patients with AKI during the index hospitalization required dialysis 90 days after the index date: 2.2% in the KPNC cohort

 TABLE 2
 Baseline Clinical Characteristics of the Fee-for-Service

 Medicare Cohort of Adults Age 66 Years or Older Undergoing
 Multivessel Coronary Revascularization

Variable	CABG (n = 52,578)	PCI (n = 52,578)	Standardized Difference
Demographics			
Age, yrs			
66-70	30.0	29.8	0.4
71-75	27.6	27.9	0.7
76-80	23.1	23.3	0.5
>80	19.3	19.0	0.8
Women	41.2	42.0	1.6
Race			
White	92.5	92.1	1.6
Black/African American	4.4	4.6	1.5
Other	3.2	3.3	1.0
Metropolitan area	73.0	73.0	0.6
U.S. census region			
New England	4.2	4.4	1.0
Middle Atlantic	12.0	12.3	0.9
South Atlantic	21.5	21.4	0.2
East South Central	7.1	7.3	0.8
West South Central	11.8	11.8	0.0
East North Central	20.2	20.1	0.2
West North Central	10.3	9.9	1.3
Mountain	4.6	4.6	0.0
Pacific	8.4	8.3	0.4
Year of procedure			
1992-1994	2.6	2.6	0.0
1995-2003	47.9	47.9	0.0
2004-2008	49.8	49.5	0.6
Comorbid conditions			
Myocardial infarction on index presentation	28.2	28.4	0.4
Tobacco abuse	18.1	19.0	2.3

TABLE 2 Continued			
	CABG	PCI	Standardized
Variable	(n = 52,578)	(n = 52,578)	Difference
Cardiovascular history			
Prior myocardial infarction	10.9	11.4	1.6
Unstable angina	30.4	29.9	1.1
Heart failure	12.5	13.2	2.1
Cerebrovascular disease	16.6	16.9	0.8
Peripheral arterial disease	17.4	18.3	2.4
Mitral/aortic valve disease	13.1	13.4	0.9
Atrial fibrillation/flutter	11.2	11.6	1.3
Ventricular fibrillation/ tachycardia	2.3	2.4	0.7
Other arrhythmia	5.4	5.6	0.9
Prior ICD	0.1	0.1	0.0
Other medical history			
Chronic kidney disease	5.4	5.5	0.4
Diabetes mellitus	33.3	33.3	0.0
Hypertension	78.5	78.6	0.2
Dyslipidemia	28.0	28.5	1.1
Depression	5.1	5.5	1.8
Dementia	3.0	3.0	0.0
Hypothyroidism	11.6	12.2	1.9
Systemic cancer	12.9	13.4	1.5
Arthritis	4.1	4.2	0.5
HIV/AIDS	0.02	0.02	0.0
Obesity	6.6	6.9	1.2
Intracranial hemorrhage	0.3	0.3	0.0
GI bleed	5.5	5.6	0.4
Chronic liver disease	1.1	1.2	0.9
Chronic lung disease	15.3	16.3	2.7
Anemia	11.8	12.2	1.2
Fluid/electrolyte	6.2	6.5	1.2

Continued in the next column

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 $\label{eq:IDS} AIDS = acquired immune deficiency syndrome; GI = gastrointestinal; HIV = human immunodeficiency virus; ICD = implantable cardioverter-defibrillator; other abbreviations as in Table 1.$

and 2.1% in the Medicare cohort. For Medicare patients who had AKI requiring dialysis during the index hospitalization, 14.9% still required dialysis at 90 days.

Our results were quite robust to the effects of potential unmeasured confounders. In the KPNC cohort, a single unmeasured confounder could account for the observed difference in odds of AKI between CABG and PCI only if it decreased the odds of AKI by at least 0.6-fold, and the prevalence of the unmeasured confounder would need to be at least 45% in the PCI group (Online Figure 3A). The results would have to be even more extreme in the Medicare cohort (Online Figure 3B). In this case, a single unmeasured confounder could account for the observed difference in odds of AKI between CABG and PCI only if it decreased the odds of AKI by at least 0.4-fold, and the prevalence of the unmeasured confounder would need to be nearly 70% in the PCI group.

DISCUSSION

Value are %.

Optimizing the decision about which type of revascularization strategy to use for multivessel coronary disease must balance the higher periprocedural morbidity and mortality risks with the long-term survival advantages of CABG compared with PCI, suggested in 2 recent studies by our group (36,37) and others (38-41). Our present analysis provides evidence from 2 separate but complementary cohorts that AKI during the index hospitalization should also be considered with the other short-term risks of CABG compared with PCI. AKI during the index hospitalization was exceptionally common after either type of coronary revascularization in our analyses, and CABG was associated with a significant 1.5- to 3-fold higher odds of AKI compared with PCI. even after accounting for differences in baseline characteristics and treatments between groups. In patients with pre-procedural CKD in both cohorts, the absolute rates of AKI were higher than in patients with preserved renal function, but the relative odds of AKI for CABG versus PCI were similar. In the Medicare cohort, although the incidence of AKI requiring dialysis was low overall, it was more common among patients with underlying CKD, and 15% of those patients still received dialysis 90 days after the index date. Thus, when considering the risks and benefits of different revascularization strategies, particular attention should be paid to patients with underlying CKD. For some patients, the risk for requiring long-term dialysis may pose such a large quality-of-life threat that they may prefer PCI, despite the shorter long-term survival associated with this strategy; the opposite may be true for other patients. Thus, an individualized, patient-centered approach to making decisions about coronary revascularization is required.

Although several studies have evaluated the incidence of AKI after either CABG or PCI separately (3,12,42-44), few studies have directly compared CABG with PCI on the risk for AKI. In a post hoc analysis using a propensity score-matched subset of the Acute Catheterization and Urgent Intervention Triage Strategy trial, participants receiving multivessel CABG or PCI, the incidence of AKI (defined as a relative 25% increase or absolute 0.5 mg/dl increase in serum creatinine) was 31.7% after CABG and 14.2% after PCI (p < 0.0001) (45). No information on baseline kidney function was reported in that trial. We extended the findings from that clinical trial to a more generalizable population of "realworld" patients by leveraging data from routine clinical practice in separate cohorts. Two studies using information from a hospital management company also showed a 2- to 4-fold higher odds of AKI after CABG compared with PCI (46,47). However, the absolute rates of AKI were very low in that study (2% to 5%), perhaps because the method of AKI ascertainment was not well defined, and no adjustments were made for differences in baseline patient characteristics.

The rates of AKI requiring dialysis were less than 1% overall in our study but between 1% and 3% for patients with pre-existing CKD, and AKI requiring dialysis was more common after CABG than PCI. Interestingly, the results from our real-world populations are consistent with results from 2 randomized clinical trials. In the Future Revascularization Evaluation in Patients With Diabetes Mellitus:

TABLE 3 Odds Ratios (95% Confidence Intervals) for Acute Kidney Injury for Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention Overall and in Selected Subgroups				
	КРМС		Medicare	
Overall	1.60 (1.30-1.96)	Overall	2.56 (2.42-2.71)	
eGFR, ml/min per 1.73 m ²		Chronic kidney disease		
≥60	1.74 (1.26-2.42)	No	2.79 (2.70-2.89)	
45-59	2.00 (1.32-2.98)	Yes	2.10 (1.89-2.33)	
<45	1.29 (0.88-1.89)			
Diabetes mellitus		Diabetes mellitus		
No	1.66 (1.25-2.21)	No	2.98 (2.89-3.10)	
Yes	1.52 (1.13-2.06)	Yes	2.14 (1.95-2.35)	
Abbreviations as in Table 1.				

Optimal Management of Multivessel Disease Trial (40), 8 patients with diabetes and multivessel coronary disease randomized to receive CABG underwent dialysis within 30 days of revascularization, compared with only 1 patient in the PCI group (p = 0.02). A post-hoc analysis of the Bypass Angioplasty Revascularization Investigation also showed a higher crude incidence of AKI requiring dialysis after multivessel CABG compared with PCI (3.2% and 2.2%, respectively) (48).

STRENGTHS AND LIMITATIONS. Our analysis has several strengths, including the use of 2 separate patient samples. The KPNC cohort had detailed



CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate in ml/min per 1.73 m²; other abbreviations as in Figure 1.



outpatient and inpatient laboratory data before the index date, allowing more accurate definition of baseline serum creatinine, which is paramount for the accurate diagnosis of AKI (19). The availability of laboratory data after the revascularization procedure allowed us to define AKI on the basis of relatively modest changes to the serum creatinine, which is a much more sensitive method than the use of administrative diagnostic codes (24). This difference in sensitivity likely accounts for the relatively higher incidence of AKI observed in the KPNC cohort than in the Medicare cohort. Patients in the communitybased KPNC cohort were very diverse in terms of race/ethnicity and age. The Medicare cohort complemented the KPNC cohort by providing a much larger sample size, allowing us to capture more cases requiring dialysis, and was drawn from a national sample of older patients.

However, our analysis also had several limitations. First, without information on coronary anatomy, we were not able to distinguish patients who underwent single-vessel PCI and then required repeat target vessel revascularization from those who underwent staged PCI procedures during the index hospitalization. We therefore included only patients who underwent multivessel revascularization within a single sitting, which could have resulted in the selection of healthier PCI patients given the higher risk nature of the procedure. We used propensity score-matching techniques to balance measured confounders between the CABG and PCI groups, but because the receipt of CABG and PCI was not randomly allocated, we cannot completely rule out residual confounding due to unmeasured factors. Moreover, we were unable to adjust for the multilevel nature of our data and thus could not account for potential differences among facilities in terms of the use of AKI-preventive strategies or ascertainment of AKI, which could lead to biased results (49). In addition, we did not have comprehensive information on the presence and severity of proteinuria in either cohort, which has been shown to be an important risk factor for AKI after coronary angiography (50). Our study period also covered a relatively long period of time, but we attempted to account for secular trends in revascularization techniques requiring an exact match on index year in our propensity score-matched cohorts. Finally, information on left ventricular ejection fraction, the use of cardiopulmonary bypass during CABG, and the amount or type of contrast material used during the PCI were unavailable, all of which may have affected the occurrence of postrevascularization AKI. However, the results of our sensitivity analyses indicate that our results were robust to the effects of any single unmeasured confounder.

CONCLUSIONS

Our study is one of the few contemporary studies to directly compare CABG with PCI on the incidence of AKI. We confirm the high incidence of AKI after coronary revascularization and show that the incidence increases with increasing severity of CKD. CABG is associated with a higher odds of AKI compared with PCI across the spectrum of CKD. Although the rates of dialysis during the index hospitalization were low, a substantial number of patients continued to require outpatient dialysis 90 days later. Because more than 1 million coronary revascularizations are performed each year in the United States (51), procedure-related AKI may account for several hundred new patients requiring maintenance dialysis each year, exacting a large physical, mental, and financial toll on patients and the health care system. Our findings underscore the need to include the risk for AKI when considering revascularization strategies for multivessel coronary disease and to continue to work to decrease the high incidence of AKI after coronary revascularization overall.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: CABG surgery is associated with greater odds of AKI than PCI in patients with multivessel coronary artery disease.

COMPETENCY IN MEDICAL KNOWLEDGE 2: Patients with CKD are at higher absolute risk for developing AKI than those without renal impairment but similar relative odds for AKI after CABG and PCI.

COMPETENCY IN INTERPERSONAL AND

COMMUNICATION SKILLS: When describing the risks and benefits of surgical intervention versus PCI in patients with multivessel coronary disease, the risk for AKI should be included, particularly for those with CKD.

TRANSLATIONAL OUTLOOK: Additional studies are needed to determine the mechanisms of postrevascularization AKI and develop more effective preventive strategies.

REFERENCES

1. Lenihan CR, Montez-Rath ME, Mora Mangano CT, Chertow GM, Winkelmayer WC. Trends in acute kidney injury, associated use of dialysis, and mortality after cardiac surgery 1999 to 2008. Ann Thorac Surg 2013;95:20-8.

2. Chertow GM, Lazarus JM, Christiansen CL, et al. Preoperative renal risk stratification. Circulation 1997;95:878-84.

3. McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. Am J Med 1997;103:368–75.

4. Siddiqui NF, Coca SG, Devereaux PJ, et al. Secular trends in acute dialysis after elective major surgery–1995 to 2009. CMAJ 2012;184:1237-45.

5. Tsai TT, Patel UD, Chang TI, et al. Contemporary incidence, predictors and outcomes of acute kidney injury in patients undergoing percutaneous coronary interventions: insights from the NCDR Cath-PCI Registry. J Am Coll Cardiol Intv 2014; 7:1-9.

6. Wi J, Ko Y-G, Kim J-S, et al. Impact of contrastinduced acute kidney injury with transient or persistent renal dysfunction on long-term outcomes of patients with acute myocardial infarction undergoing percutaneous coronary intervention. Heart 2011;97:1753-7.

7. James MT, Samuel SM, Manning MA, et al. Contrast-induced acute kidney injury and risk of adverse clinical outcomes after coronary angiography: a systematic review and meta-analysis. Circ Cardiovasc Interv 2013;6:37-43.

8. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol 2005;16:3365-70.

9. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol 2009;20:223-8.

10. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. Kidney Int 2012;81:442–8.

11. Maioli M, Toso A, Leoncini M, Gallopin M, Musilli N, Bellandi F. Persistent renal damage after contrast-induced acute kidney injury: incidence, evolution, risk factors, and prognosis. Circulation 2012;125:3099-107.

12. Huang T-M, Wu V-C, Young G-H, et al. Preoperative proteinuria predicts adverse renal outcomes after coronary artery bypass grafting. J Am Soc Nephrol 2011;22:156-63.

13. Krieger N. Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. Am J Public Health 1992;82:703-10.

14. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.

15. Ming K, Rosenbaum PR. Substantial gains in bias reduction from matching with a variable number of controls. Biometrics 2000;56:118-24.

16. Kosanke J, Bergstralh E. GMATCH macro: match 1 or more controls to cases using the GREEDY algorithm. Rochester, Minnesota: Mayo Clinic College of Medicine, 2004.

17. Parsons L. Reducing bias in a propensity score matched-pair sample using greedy matching techniques (paper 214-26). Paper presented at: 26th Annual SAS Users Group International Conference; 2001; Long Beach, CA.

18. Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clin Chem 2007;53:766-72.

19. Go AS, Parikh CR, Ikizler TA, et al. The Assessment, Serial Evaluation, and Subsequent Sequelae of Acute Kidney Injury (ASSESS-AKI) study: design and methods. BMC Nephrol 2010;11:22.

20. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.

21. Winkelmayer WC, Schneeweiss S, Mogun H, Patrick AR, Avorn J, Solomon DH. Identification of

individuals with CKD from Medicare claims data: a validation study. Am J Kidney Dis 2005;46: 225-32.

22. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.

23. Slocum NK, Grossman PM, Moscucci M, et al. The changing definition of contrast-induced nephropathy and its clinical implications: insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). Am Heart J 2012; 163:829–34.

24. Waikar SS, Wald R, Chertow GM, et al. Validity of International Classification of Diseases, Ninth Revision, Clinical Modification codes for acute renal failure. J Am Soc Nephrol 2006;17:1688-94.

25. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296-305.

26. Go AS, Lee WY, Yang J, Lo JC, Gurwitz JH. Statin therapy and risks for death and hospitalization in chronic heart failure. JAMA 2006;296: 2105–11.

27. Selby JV, Ray GT, Zhang D, Colby CJ. Excess costs of medical care for patients with diabetes in a managed care population. Diabetes Care 1997; 20:1396–402.

28. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285: 2486–97.

29. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145:247-54.

30. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1-266.

31. Fireman BH, Fehrenbacher L, Gruskin EP, Ray GT. Cost of care for patients in cancer clinical trials. J Natl Cancer Inst 2000;92:136-42.

32. Go AS, Yang J, Gurwitz JH, Hsu J, Lane K, Platt R. Comparative effectiveness of different beta-adrenergic antagonists on mortality among adults with heart failure in clinical practice. Arch Intern Med 2008;168:2415-21.

33. Go AS, Yang J, Ackerson LM, et al. Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) study. Circulation 2006;113: 2713-23.

34. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083-107.

35. Lin DY, Psaty BM, Kronmal RA. Assessing the sensitivity of regression results to unmeasured confounders in observational studies. Biometrics 1998;54:948–63.

36. Hlatky MA, Boothroyd DB, Baker L, et al. Comparative effectiveness of multivessel coronary bypass surgery and multivessel percutaneous coronary intervention: a cohort study. Ann Intern Med 2013;158:727-34.

37. Chang TI, Leong TK, Kazi DS, Lee HS, Hlatky MA, Go AS. Comparative effectiveness of coronary artery bypass grafting and percutaneous coronary intervention for multivessel coronary disease in a community-based population with chronic kidney disease. Am Heart J 2013;165:800–8. **38.** Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. N Engl J Med 2012;366:1467-76.

39. Hlatky MA, Boothroyd DB, Bravata DM, et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. Lancet 2009;373:1190–7.

40. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012;367:2375-84.

41. Cohen DJ, Van Hout B, Serruys PW, et al. Quality of life after PCI with drug-eluting stents or coronary-artery bypass surgery. N Engl J Med 2011;364:1016-26.

42. Mehta RH, Honeycutt E, Patel UD, et al. Impact of recovery of renal function on long-term mortality after coronary artery bypass grafting. Am J Cardiol 2010;106:1728-34.

43. Nicoara A, Patel UD, Phillips-Bute BG, et al. Mortality trends associated with acute renal failure requiring dialysis after CABG surgery in the United States. Blood Purif 2009;28:359–63.

44. Rihal CS, Textor SC, Grill DE, et al. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. Circulation 2002;105:2259-64.

45. Ben-Gal Y, Moses JW, Mehran R, et al. Surgical versus percutaneous revascularization for multivessel disease in patients with acute coronary syndromes: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. J Am Coll Cardiol Intv 2010;3:1059-67.

46. Mack MJ, Brown PP, Kugelmass AD, et al. Current status and outcomes of coronary revascularization 1999 to 2002:148,396 surgical and percutaneous procedures. Ann Thorac Surg 2004; 77:761-8.

47. Mack MJ, Prince SL, Herbert M, et al. Current clinical outcomes of percutaneous coronary intervention and coronary artery bypass grafting. Ann Thorac Surg 2008;86:496-503.

48. Szczech LA, Best PJ, Crowley E, et al. Outcomes of patients with chronic renal insufficiency in the bypass angioplasty revascularization investigation. Circulation 2002;105:2253-8.

49. Griswold ME, Localio AR, Mulrow C. Propensity score adjustment with multilevel data: setting your sites on decreasing selection bias. Ann Intern Med 2010;152:393-5.

50. James MT, Ghali WA, Knudtson ML, et al. Associations between acute kidney injury and cardiovascular and renal outcomes after coronary angiography/clinical perspective. Circulation 2011; 123:409–16.

51. Epstein AJ, Polsky D, Yang F, Yang L, Groeneveld PW. Coronary revascularization trends in the United States 2001-2008. JAMA 2011;305: 1769–76.

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APPENDIX For supplemental tables and figures, please see the online version of this article.