Estimating the Risk of Radiocontrast-Associated Nephropathy

Emilee Wilhelm-Leen, Maria E. Montez-Rath, and Glenn Chertow

Department of Medicine, Division of Nephrology, Stanford University School of Medicine, Palo Alto, California

ABSTRACT

Estimates of the incidence of radiocontrast-associated nephropathy vary widely and suffer from misclassification of the cause of AKI and confounding. Using the Nationwide Inpatient Sample, we created multiple estimates of the risk of radiocontrast-associated nephropathy among adult patients hospitalized in the United States in 2009. First, we stratified patients according to the presence or absence of 12 relatively common diagnoses associated with AKI and evaluated the rate of AKI between strata. Next, we created a logistic regression model, controlling for comorbidity and acuity of illness, to estimate the risk of AKI associated with radiocontrast administration within each stratum. Finally, we performed an analysis stratified by the degree of preexisting comorbidity. In general, patients who received radiocontrast did not develop AKI at a clinically significant higher rate. Adjusted only for the complex survey design, patients to whom radiocontrast was and was not administered developed AKI at rates of 5.5% and 5.6%, respectively. After controlling for comorbidity and acuity of illness, radiocontrast administration associated with an odds ratio for AKI of 0.93 (95% confidence interval, 0.88 to 0.97). In conclusion, the risk of radiocontrast-associated nephropathy may be overstated in the literature and overestimated by clinicians. More accurate AKI risk estimates may improve clinical decision-making when attempting to balance the potential benefits of radiocontrast-enhanced imaging and the risk of AKI.

J Am Soc Nephrol 28: ●●●–●●●, 2016. doi: 10.1681/ASN.2016010021

Iodinated radiocontrast agents have been known for decades to cause AKI when administered intravenously or intra-arterially. A widely cited paper published in 2002 suggested that contrast-associated nephropathy (CAN), also commonly referred to as contrast-induced nephropathy, is the third most common cause of AKI in hospitalized patients.[1] Clinical definitions and diagnostic criteria vary somewhat, but generally, CAN is considered to be present when a patient receives radiocontrast for an imaging study, either intravenously or intra-arterially, and subsequently demonstrates a rise in the serum creatinine concentration of either 44 μmol/L (0.5 mg/dl) or a 25% increase from baseline over the ensuing 24–72 hours. The diagnosis is notably one of exclusion and can only be made if AKI cannot reasonably be attributed to another etiology.

There is little agreement in the medical literature regarding the incidence of CAN. Published rates range from $<$1% to $>$30%.[2–6] In fact, at least two prospective studies failed to show any increase in the rate of AKI in patients receiving radiocontrast when compared with materially similar patients who did not receive radiocontrast.[7,8] Although efforts were undertaken in both studies to match controls to cases, residual confounding renders these results difficult to interpret. Patients receiving radiocontrast are generally sicker than those who do not receive radiocontrast; conversely, patients with diminished kidney function or those patients perceived by their physicians to be at increased risk for AKI (*e.g.*, older persons, or persons

Received January 7, 2016. Accepted July 12, 2016.

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Emilee Wilhelm-Leen, Stanford University School of Medicine, Department of Medicine, Division of Nephrology, 1070 Arastradero Road, Palo Alto, CA 94304. Email: ewilhelm@stanford.edu

with underlying CKD or diabetes mellitus) may be less likely to receive radiocontrast.[9] Indirect evidence from studies that evaluate fluctuations in serum creatinine absent the administration of radiocontrast also suggests that published incidence rates of CAN may be inflated. For example, a recently published study reported a high incidence of transient creatinine fluctuations in hospitalized patients who had not received radiocontrast.[10,11] Another study compared rates of transient creatinine fluctuation among patients receiving radiocontrast and nonradiocontrast computed tomography (CT) scans and noted an increased risk of AKI among patients who did not undergo a radiocontrast study when compared with those receiving the radiocontrast agent iohexol.[10] Recently, McDonald *et al.* published the results of a large retrospective analysis that employed propensity score matching to compare risk of AKI after contrast and noncontrast-enhanced CT scanning; they found no increase in the incidence of AKI after administration of intravenous contrast, even among high risk groups (for example, patients with baseline CKD or diabetes mellitus).[12]

In this study, we sought to estimate the burden of AKI among patients receiving radiocontrast, as compared with patients with similar comorbidity and severity of illness who did not receive radiocontrast during their hospitalization. We hypothesized that the risk of AKI in patients who received radiocontrast would not be dramatically different from the risk in patients who did not receive radiocontrast.

RESULTS

Study Sample

The entire Nationwide Inpatient Sample (NIS) dataset for 2009 consisted of 7,810,762 hospitalizations. After restricting our sample to hospitalizations for patients older than 18 years with lengths of stay 10 days or fewer, we were left with 5,931,523 hospitalizations for analysis (Figure 1).

Study Subject Characteristics

Figure 2 summarizes demographic and comorbidity data for the study sample. Patients receiving radiocontrast were older, disproportionately male, and more likely to be white. Radiocontrast was more commonly administered at teaching hospitals. Patients not receiving radiocontrast had a higher comorbidity score.

Risk of AKI

In the entire sample, AKI developed in 5.5% of patients who received radiocontrast and 5.6% of patients who did not. In the stratified analyses, for some disease states (Table 1), radiocontrast administration was associated with a higher risk of AKI: sepsis (35.8% versus 32.9%), pneumonia (16.3% versus 12.7%), urinary tract infection/pyelonephritis (17.4% versus 15.7%), peritonitis (31.4% versus 28.9%), gastrointestinal bleeding (16.8% versus 13.8%), chronic obstructive pulmonary disease exacerbation (16.3% versus 15.1%), and acute pancreatitis (16.4% versus 8.2%). In general, differences in

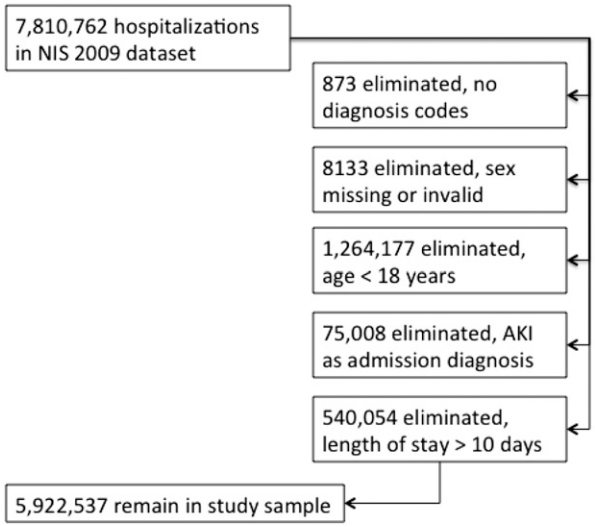

Figure 1. Assembly of the cohort of included hospitalizations from the total sample.

risk between groups were small, roughly 2%–3% absolute, 15%–20% relative. The notable exception was acute pancreatitis; for these patients radiocontrast administration was associated with a doubling in risk of AKI. For several other disease states, patients who received radiocontrast experienced an unexpectedly lower rate of AKI: heart failure exacerbation (16.6% versus 19.0%), endocarditis (16.4% versus 19.9%), acute coronary syndrome (ACS) (6.4% versus 17.4%), venous thromboembolism (6.9% versus 9.2%), and stroke/cerebrovascular accident (6.7% versus 7.5%). These results are summarized in Table 2 and depicted graphically in Figure 3.

In the unadjusted model (adjusted only for survey design), the administration of radiocontrast was associated with a nonsignificant 2% lower odds of AKI; the discrimination of this model was poor (concordance statistic [c-statistic], 0.50). Adjusted for age, sex, mechanical ventilation, and comorbidity, the administration of radiocontrast was associated with a 7.4% (95% confidence interval, 2.6% to 12.0%) reduction in the odds of AKI. Model discrimination was very good (c-statistic, 0.82) (Table 3). These results suggest a negligible to at most modest increase in risk attributable to radiocontrast.

Finally, we performed an analysis stratified for degree of comorbidity (Table 4). The risk of AKI was higher with higher comorbidity scores in both groups (exposed and not exposed to radiocontrast).

DISCUSSION

Using a dataset that contains 8,000,000 hospitalizations, representing 96% of the United States population, our analyses suggest that the incremental risk of AKI that can be attributed to radiocontrast is modest at worst, and almost certainly overestimated by patients, physicians, surgeons, radiologists, and other decision-makers. This relation between radiocontrast

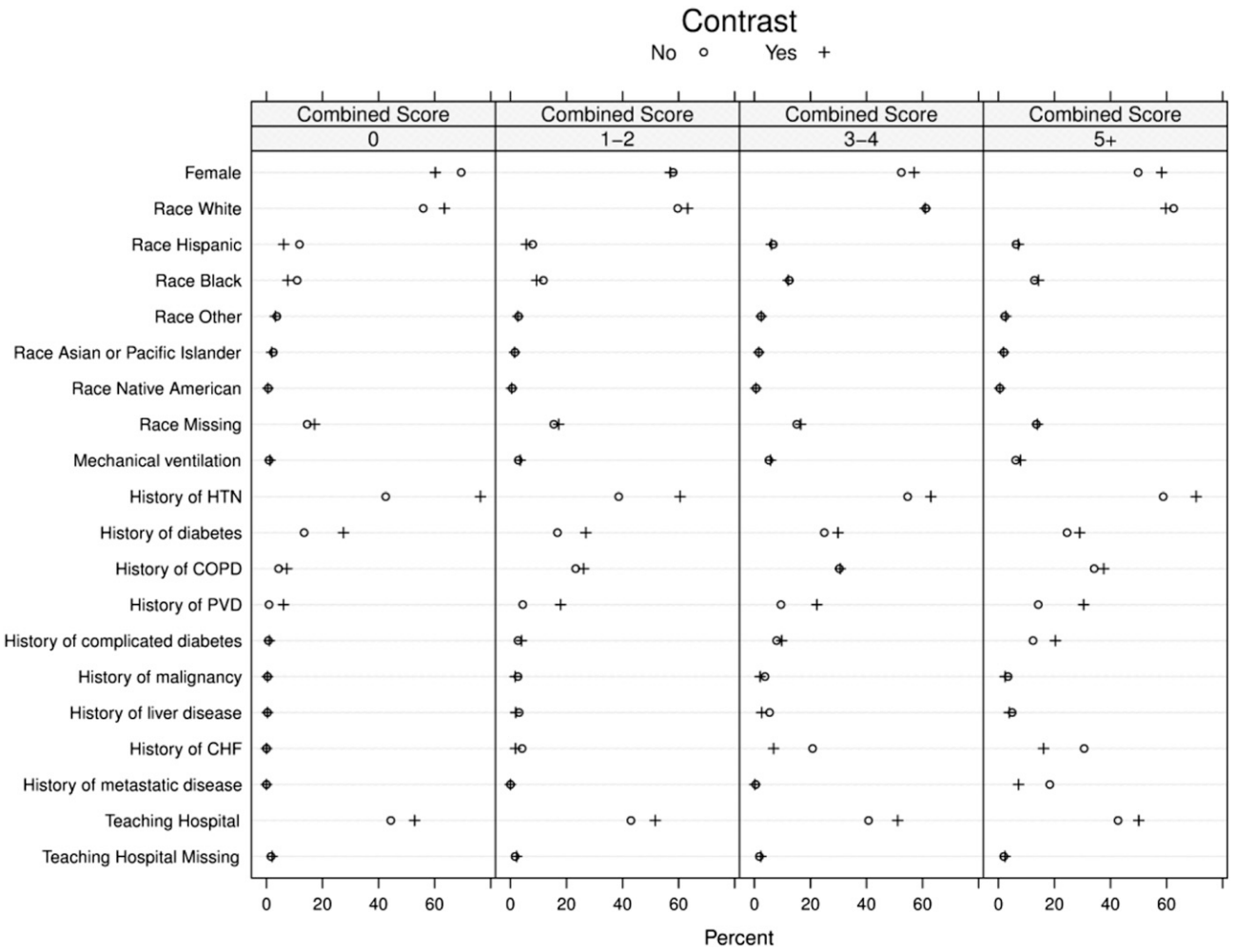

Figure 2. The relationship between contrast administration, demographic data, and clinical characteristics for each level of co-morbidity burden. Demographic and clinical characteristics of the study sample, stratified by comorbidity score.

exposure and AKI varies according to total comorbidity and acuity of illness, and is modified by the presence of specific disease states. For example, across the entire hospitalized adult population, adjusting only for the complex survey design, the risk of AKI in patients receiving and not receiving radiocontrast was virtually identical (5.5% versus 5.6%, respectively) and notably similar to other published reports.[13] Similarly, when controlling for demographic features, mechanical ventilation, and a previously validated combined comorbidity score, radiocontrast administration is associated with 7% lower (relative) odds of AKI. Taken together, these surprising results suggest that the risk of AKI that can reasonably be attributed to radiocontrast (the so-called "attributable risk") is likely to be much lower than frequently assumed.

Data from the disease-specific strata offer additional insight. For example, the risk of AKI among persons with ACS (including ST segment elevation and non-ST segment elevation myocardial infarction and unstable angina) who receive radiocontrast is actually lower, and considerably so, than among those patients who did not receive a radiocontrast study. It is very unlikely that radiocontrast "protects" patients with ACS from developing AKI. Rather, this paradox could be explained by the fact that patients who are deemed by clinicians to be at highest risk for AKI are treated in such a way as to minimize perceived risk. Indeed, clinically indicated angiographic studies may be delayed or withheld.[9] In contrast, the opposite pattern is seen for patients with acute pancreatitis, a condition where most patients do not receive a radiocontrast study as part of standard of care. However, with persistent fever, pain, and leukocytosis, radiocontrast-enhanced CT may be indicated to investigate the possibility of pancreatic necrosis or the development of a phlegmon or other complication. Therefore, although in the setting of pancreatitis the risk of AKI doubled with radiocontrast exposure, much of that observed increased risk could be attributed to other causes, and yet radiocontrast might be "blamed."

As is evidenced from the discussion above, determination of the true rate of CAN would be very difficult even if more detailed clinical data were available. Simply put, the relation between radiocontrast administration and AKI is highly

Table 1. ICD9 codes used to define clinical conditions

Disease State	ICD9 Code
Primary outcome	
AKI	584.5, 584.6, 584.7, 584.8, 584.9
Primary independent variable	
Contrast administration	88.4, 88.5, 88.6
Exacerbation of chronic disease	
CHF	428.21, 428.23, 428.31, 428.33, 428.41, 428.43
Chronic lung disease	518.84
Infection	
Sepsis/bacteremia	995.91, 995.92
PNA	480, 481, 482, 483, 484, 485, 486
UTI/pyelonephritis	599.0, 590.1
Peritonitis	567.23
Endocarditis	421
Other	
VTE (PE and DVT)	453.4, 453.8, 453.9, 415.1
ACS	410, 411
CVA	431, 434
GI bleeding	578
Acute pancreatitis	570.0

CHF, congestive heart failure; PNA, pneumonia; UTI, urinary tract infection; VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep venous thrombosis; CVA, cerebrovascular accident; GI, gastrointestinal.

confounded, unpredictable, and sometimes bidirectional. Sicker patients typically require more extensive and defined imaging studies, although in some settings, patients considered to be at high risk for AKI may be less likely to undergo radiocontrast-enhanced testing. This potentially bidirectional relationship may underlie our potentially counterintuitive result seen in Table 4; although the rate of AKI increases as the combined comorbidity score increases in both the contrast and noncontrast groups, the odds of AKI are actually greater in the noncontrast groups among persons with a combined comorbidity score of less than five. This pattern may primarily reflect patient selection: among low risk patients, physicians identify patients at high risk for AKI and administer contrast accordingly; however, for the sickest patients in whom the risk of AKI is greatest, there may be less perceived choice about the administration of contrast which, in the case of the sickest patients, may be life-saving.

It will not be feasible to randomize patients to contrast-enhanced versus noncontrast-enhanced imaging strategies, leaving all other care unchanged, to determine the degree to which radiocontrast directly increases AKI risk, although some sophisticated study designs and analyses can come close. Most notably, in a series of influential papers, McDonald and colleagues assembled a retrospective, single-site cohort of patients undergoing either intravenous contrast-enhanced CT imaging or noncontrast-enhanced CT.[12,14,15] The researchers limited the sample to patients with sufficient data to assess baseline kidney function and relevant comorbidities, as well as determine the rate of AKI in the 24–72 hours after imaging. Secondary outcomes including death or dialysis within 30 days of imaging were also evaluated. The analysis took a multipronged approach including stratification on the basis of baseline kidney function, use of propensity score for adjustment and a 1:1 matching analysis, and an elegant counterfactual analysis taking advantage of the fact that many patients received both contrast-enhanced and noncontrast studies at different time points, thus providing

Table 2. Risk of AKI, entire sample and diagnosis-defined strata

Population	No Contrast (*n*=28,272,751)	Contrast (*n*=1,667,694)	*P* Value
Entire sample (*n*=29,940,445)	5.6 (5.4 to 5.8)	5.5 (5.2 to 5.8)	0.51
Cardiac			
CHF exacerbation (*n*=804,846)	19.0 (18.3 to 19.8)	16.6 (15.7 to 17.6)	<0.001
ACS (*n*=1,251,812)	17.4 (16.6 to 18.1)	6.4 (6.0 to 6.8)	<0.001
Infectious			
Sepsis (*n*=773,258)	32.9 (32.2 to 33.6)	35.8 (33.8 to 37.8)	0.003
Pneumonia (*n*=1,946,602)	12.7 (12.3 to 13.2)	16.3 (15.3 to 17.5)	<0.001
UTI (*n*=2,221,705)	15.7 (15.3 to 16.2)	17.4 (16.5 to 18.4)	0.001
Peritonitis (*n*=12,466)	28.9 (26.6 to 31.2)	31.4 (11.6 to 61.5)	0.85
Endocarditis (*n*=21,376)	19.9 (18.7 to 21.1)	16.4 (12.2 to 21.8)	0.20
Vascular			
CVA (*n*=504,144)	7.5 (7.2 to 7.8)	6.7 (6.1 to 7.5)	0.03
VTE (*n*=66,330)	9.2 (8.7 to 9.8)	6.9 (5.7 to 8.2)	0.001
GIB (*n*=457,195)	13.8 (13.4 to 14.3)	16.8 (15.4 to 18.3)	<0.001
Other			
COPD exacerbation (*n*=175,134)	15.1 (14.4 to 15.9)	16.3 (13.8 to 19.2)	0.38
Pancreatitis (*n*=373,154)	8.2 (7.8 to 8.5)	16.4 (13.6 to 19.5)	<0.001

Data displayed as % AKI (95% confidence interval). CHF, congestive heart failure; UTI, urinary tract infection; CVA, cerebrovascular accident; VTE, venous thromboembolism; GIB, gastrointestinal bleeding; COPD, chronic obstructive pulmonary disease.

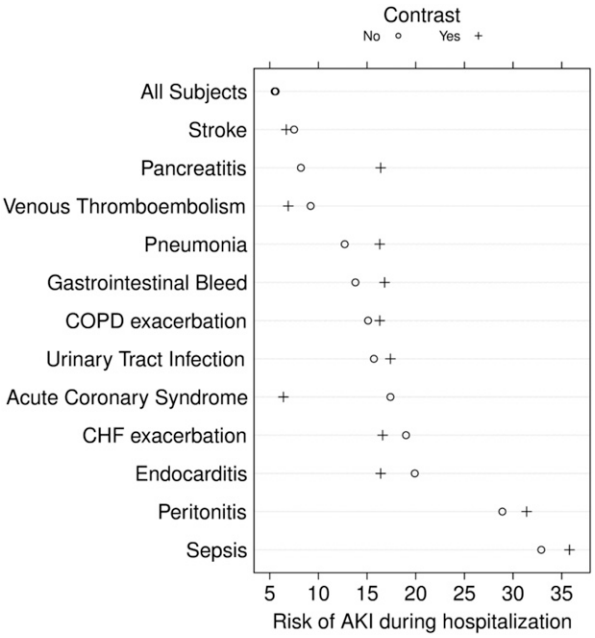

Figure 3. The variable relationship between contrast administration and AKI across the examined disease states. Risk of AKI, entire sample and diagnosis-defined strata.

their own control. Rates of AKI, death, and dialysis were roughly similar to previously published reports but did not differ significantly between the contrast and noncontrast group in any analysis variation. Our study affirms and builds on this important work: despite a different data source and analytic methods, our result is materially similar. Given that this result may run counter to longstanding physician beliefs about the risk of radiocontrast and practices related to those beliefs, it is important to confirm a potentially controversial and practice-changing result in multiple studies and settings.

The strengths of our study include the use of a very large and nationally representative dataset that contains data for all payers, the only dataset of its kind in the United States. Our study also benefits from two separate analyses (stratified by disease state and logistic regression model controlled for comorbidity and acuity of illness), each in an effort to illuminate the problem of making a meaningful comparison of two intrinsically different patient groups (*i.e.,* those who do and do not receive radiocontrast). The results were consistent, another strength when considering interpretation of our results.

Our data source, although large and nationally representative, carries several important limitations. First, the definition of AKI is based exclusively on administrative diagnosis codes which are likely to be less sensitive for the identification of AKI than clinical data. However, we report an overall rate of AKI very similar to studies which used clinical data to identify AKI. Second, as discussed in detail in our Concise Methods section, we were unable to determine with certainty that the administration of contrast preceded the diagnosis of AKI within any particular hospitalization. We have mitigated this risk by limiting our analysis to relatively short hospitalizations but the issue could not be completely eliminated; this is a weakness intrinsic to the dataset itself.

The value gained and the risk incurred by imaging studies in general, and radiocontrast-enhanced imaging studies in particular, remain critically important questions in general medical and surgical care, cardiology, oncology, and other medical and surgical subspecialties. Indeed, the US Department of Veterans Affairs Cooperative Studies Program and the George Institute recently launched a large randomized clinical trial of two prophylactic strategies aimed to reduce the risk of radiocontrast nephropathy after angiography. Unfortunately, because all participants in the Veterans Affairs Cooperative Study will be exposed to radiocontrast, the trial will not determine the degree to which radiocontrast increases the risk of AKI. Although we await additional prospective data, we suspect that, on the basis of existing assumptions regarding attributable risk, diagnostic studies and some interventions that might save or improve lives are being withheld from patients owing to an exaggerated fear of radiocontrast nephropathy.

However, we would also extend a word of caution regarding interpretation of these results and results from similar studies: to date there have been no randomized studies of the risk of radiocontrast administration. Even sophisticated analyses may fail to detect the full effect of patient selection on their results and, in that case, may erroneously conclude that there is no real risk to patients, even those previously believed to be high risk such as patients with CKD or diabetes. If physicians are expertly identifying patients truly at increased risk for AKI after radiocontrast administration, that selection bias may mask a true effect of contrast in analyses such as ours and the study performed by McDonald *et al.*[12] For this reason, we must interpret this study and similar studies with caution, carefully weighing the benefit of a contrast-enhanced study with the risk, likely low but likely not zero, of radiocontrast administration on the kidney.

Table 3. Odds of AKI after contrast administration

	Unadjusted Model		Adjusted[a] Model	
	Odds Ratio	Adjusted Percentages	Odds Ratio	Adjusted Percentages
No contrast	Reference	5.6 (5.4–5.8)	Reference	5.6 (5.4–5.8)
Contrast	0.98 (0.93–1.04)	5.5 (5.2–5.8)	0.93 (0.88–0.97)	5.1 (4.9–5.4)
c-statistic	0.50		0.81	

[a]Model adjusted for age, sex, mechanical ventilation, and combined comorbidity score. Parentheses contain 95% confidence intervals.

Table 4. Odds of AKI after contrast administration, stratified by preexisting comorbidity

CCS	Odds Ratio[a]	Adjusted Percentages		Adjusted Difference, %	c-Statistic[b]
		No Contrast	Contrast		
0 (*n*=14,277,527)	0.57 (0.52–0.62)	1.4	0.8	−0.6 (−0.7– −0.5)	0.75
1–2 (*n*=9,105,123)	0.78 (0.74–0.83)	4.8	3.8	−1.0 (-1.2– −0.7)	0.67
3–4 (*n*=3,666,390)	0.82 (0.78–0.87)	13.1	11.1	−2.0 (-2.5– −1.5)	0.57
5 (*n*=2,891,405)	1.17 (1.12–1.23)	19.9	22.5	2.6 (1.7–3.4)	0.0

CCS, combined comorbidity score. Parentheses contain 95% confidence intervals.
[a]Model adjusted for age, sex, and mechanical ventilation.
[b]c-statistic computed from a weighted logistic regression model.

CONCISE METHODS

Data Source and Study Population

Data for this study were drawn from the NIS, the largest publicly available all-payer inpatient care database in the United States. The NIS is a 20% stratified sample of discharges from United States hospitals; the sample contains administrative data from approximately 8,000,000 hospitalizations per year. More than 1000 hospitals contribute to the database, from 45 states, representing 96% of the United States population. Sample weights are provided to allow the generation of national estimates. The NIS was developed as part of the family of databases that comprise the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality.

For these analyses, we utilized the 2009 subset, the most recent year available at the time of data analysis. We included patients at least 18 years old at the time of admission with an admitting diagnosis other than AKI. We limited our study population to those hospitalizations 10 days or fewer in length to reduce misclassification of CAN (Figure 1).

Study Variables

The NIS, although enormously powerful given its very large size, has several notable limitations. First, the NIS contains no detailed clinical or laboratory data; therefore, we relied on administrative data to identify the dependent variable (AKI), the key independent variable (radiocontrast exposure), and other covariates. Second, the number of diagnoses and procedures listed for any single hospitalization is limited; the dataset contains up to 25 diagnosis codes and up to 15 procedure codes for each hospitalization. Third, procedure and diagnosis codes have no associated dates, preventing us from determining the sequence of events within each hospitalization. Finally, because there are no patient identifiers, multiple hospitalizations within individual patients cannot be tracked. Given that administration of radiocontrast before the diagnosis of AKI is central to the diagnosis of CAN, this imprecision in the data represents a major limitation. We addressed this limitation by restricting our study sample to hospitalizations lasting 10 days or fewer, reducing the likelihood that we would include a hospitalization in our analysis where radiocontrast preceded AKI but was separated by an extended time period (indicating AKI from another cause) or where radiocontrast was administered after the development of AKI, where it might contribute to, but not incite, the event.

The primary outcome for our study was AKI, as determined by International Classification of Diseases, 9th Revision Codes (ICD9) diagnosis code. The primary independent variable was radiocontrast administration, as determined by ICD9 procedure code. Covariates included age, sex, the Romano implementation of the combined Charlson/Elixhauser comorbidity index, and the presence or absence of a procedure code for mechanical ventilation to control for acuity of illness. The combined comorbidity index included ICD9 diagnosis codes to identify myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, liver disease, diabetes, hemi/paraplegia, renal disease, malignancy including metastatic disease, and AIDS.[16] Additional analyses were conducted on samples stratified by 12 disease states: heart failure exacerbation, chronic obstructive pulmonary disease exacerbation, sepsis, pneumonia, urinary tract infection/pyelonephritis, endocarditis, peritonitis, venous thromboembolism including deep venous thrombosis and pulmonary embolism, ACS, stroke/cerebrovascular accident, acute pancreatitis, and gastrointestinal bleeding. A full list of ICD9 codes employed in the analysis are summarized in Table 1.

Statistical Analyses

Characteristics of patients who did and did not receive radiocontrast were compared using the median (interquartile range) for continuous variables (age) and percentages for categoric variables. We compared the risk of AKI for patients who did and did not receive contrast among the entire sample and stratified by the disease states listed above using the chi-squared test for statistical significance. We compared the odds of AKI as a function of contrast administration by fitting logistic regression models. We fitted unadjusted and multivariable-adjusted models; the latter adjusted for age, sex, combined comorbidity, and mechanical ventilation. We gauged model discrimination by the area of the receiver operating characteristic curve, depicted with the c-statistic. For a more intuitive interpretation of this model, we additionally calculated the predicted marginal percentages and differences for the risk of AKI associated with contrast administration, stratified by degree of preexisting comorbidity. The predicted marginal percent for contrast/no contrast categories represents the average predicted response assuming that all covariates in the contrast category are distributed similarly to the whole population. All analyses presented account for the complex survey design (weighting and stratification) and subpopulation estimation using survey-specific procedures in the Statistical Analysis System (SAS) and variables for strata and weights as provided by the HCUP to allow for accurate national estimates. We created the cohort using SAS software, version 9.3 (SAS Institute Inc., Cary, NC); and we conducted the analyses using StataMP, version 12 (Stata Corp., College Station, TX).

DISCLOSURES

None.

REFERENCES

1. Nash K, Hafeez A, Hou S: Hospital-acquired renal insufficiency. *Am J Kidney Dis* 39: 930–936, 2002
2. Josephson SA, Dillon WP, Smith WS: Incidence of contrast nephropathy from cerebral CT angiography and CT perfusion imaging. *Neurology* 64: 1805–1806, 2005
3. Asif A, Cherla G, Merrill D, Cipleu CD, Tawakol JB, Epstein DL, Lenz O: Venous mapping using venography and the risk of radiocontrast-induced nephropathy. *Semin Dial* 18: 239–242, 2005
4. Ng CS, Shaw AD, Bell CS, Samuels JA: Effect of IV contrast medium on renal function in oncologic patients undergoing CT in ICU. *AJR Am J Roentgenol* 195: 414–422, 2010
5. Pahade JK, LeBedis CA, Raptopoulos VD, Avigan DE, Yam CS, Kruskal JB, Pedrosa I: Incidence of contrast-induced nephropathy in patients with multiple myeloma undergoing contrast-enhanced CT. *AJR Am J Roentgenol* 196: 1094–1101, 2011
6. Lufft V, Hoogestraat-Lufft L, Fels LM, Egbeyong-Baiyee D, Tusch G, Galanski M, Olbricht CJ: Contrast media nephropathy: intravenous CT angiography versus intraarterial digital subtraction angiography in renal artery stenosis: a prospective randomized trial. *Am J Kidney Dis* 40: 236–242, 2002
7. Cramer BC, Parfrey PS, Hutchinson TA, Baran D, Melanson DM, Ethier RE, Seely JF: Renal function following infusion of radiologic contrast material. A prospective controlled study. *Arch Intern Med* 145: 87–89, 1985
8. Heller CA, Knapp J, Halliday J, O'Connell D, Heller RF: Failure to demonstrate contrast nephrotoxicity. *Med J Aust* 155: 329–332, 1991
9. Chertow GM, Normand SL, McNeil BJ: "Renalism": inappropriately low rates of coronary angiography in elderly individuals with renal insufficiency. *J Am Soc Nephrol* 15: 2462–2468, 2004
10. Bruce RJ, Djamali A, Shinki K, Michel SJ, Fine JP, Pozniak MA: Background fluctuation of kidney function versus contrast-induced nephrotoxicity. *AJR Am J Roentgenol* 192: 711–718, 2009
11. Newhouse JH, Kho D, Rao QA, Starren J: Frequency of serum creatinine changes in the absence of iodinated contrast material: implications for studies of contrast nephrotoxicity. *AJR Am J Roentgenol* 191: 376–382, 2008
12. McDonald JS, McDonald RJ, Carter RE, Katzberg RW, Kallmes DF, Williamson EE: Risk of intravenous contrast material-mediated acute kidney injury: a propensity score-matched study stratified by baseline-estimated glomerular filtration rate. *Radiology* 271: 65–73, 2014
13. McDonald JS, McDonald RJ, Comin J, Williamson EE, Katzberg RW, Murad MH, Kallmes DF: Frequency of acute kidney injury following intravenous contrast medium administration: a systematic review and meta-analysis. *Radiology* 267: 119–128, 2013
14. McDonald RJ, McDonald JS, Carter RE, Hartman RP, Katzberg RW, Kallmes DF, Williamson EE: Intravenous contrast material exposure is not an independent risk factor for dialysis or mortality. *Radiology* 273: 714–725, 2014
15. McDonald RJ, McDonald JS, Bida JP, Carter RE, Fleming CJ, Misra S, Williamson EE, Kallmes DF: Intravenous contrast material-induced nephropathy: causal or coincident phenomenon? *Radiology* 267: 106–118, 2013
16. Romano PS, Roos LL, Jollis JG: Adapting a clinical comorbidity index for use with ICD-9-CM administrative data: differing perspectives. *J Clin Epidemiol* 46: 1075–1079, discussion 1081–1090, 1993