

# Incidence and Outcomes of Contrast-Induced AKI Following Computed Tomography

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**Background and objectives:** Most studies of contrast-induced acute kidney injury (CIAKI) have focused on patients undergoing angiographic procedures. The incidence and outcomes of CIAKI in patients undergoing nonemergent, contrast-enhanced computed tomography in the inpatient and outpatient setting were assessed.

**Design, setting, participants, & measurements:** Patients with estimated glomerular filtration rates (GFRs) <60 ml/min per 1.73 m<sup>2</sup> undergoing nonemergent computed tomography with intravenous iodinated radiocontrast at an academic VA Medical Center were prospectively identified. Serum creatinine was assessed 48 to 96 h postprocedure to quantify the incidence of CIAKI, and the need for postprocedure dialysis, hospital admission, and 30-d mortality was tracked to examine the associations of CIAKI with these medical outcomes.

**Results:** A total of 421 patients with a median estimated GFR of 53 ml/min per 1.73 m<sup>2</sup> were enrolled. Overall, 6.5% of patients developed an increase in serum creatinine  $\geq 25\%$ , and 3.5% demonstrated a rise in serum creatinine  $\geq 0.5$  mg/dl. Although only 6% of outpatients received preprocedure and postprocedure intravenous fluid, <1% of outpatients with estimated GFRs >45 ml/min per 1.73 m<sup>2</sup> manifested an increase in serum creatinine  $\geq 0.5$  mg/dl. None of the study participants required postprocedure dialysis. Forty-six patients (10.9%) were hospitalized and 10 (2.4%) died by 30-d follow-up; however, CIAKI was not associated with these outcomes.

**Conclusions:** Clinically significant CIAKI following nonemergent computed tomography is uncommon among outpatients with mild baseline kidney disease. These findings have important implications for providers ordering and performing computed tomography and for future clinical trials of CIAKI.

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The intravascular administration of iodinated contrast media is a well-recognized cause of acute kidney injury, which in turn, is associated with in-hospital morbidity and mortality (1–4). Clinical factors that increase the risk for contrast-induced acute kidney injury (CIAKI) include pre-existing kidney disease, diabetes mellitus in the setting of underlying renal impairment, advanced congestive heart failure, intravascular volume depletion, administration of large volumes of contrast, and the use of high-osmolal contrast media (1,5–8). Much of our understanding of the risk factors for, incidence of, and outcomes associated with CIAKI emanate from clinical studies of patients undergoing angiography, particularly coronary angiography. Moreover, most clinical trials of preventive interventions, such as N-acetylcysteine (NAC) and intravenous (IV) fluids, have been conducted in patients

undergoing angiographic procedures (9–15). Despite this, expert recommendations for the prevention of CIAKI make little distinction between patients undergoing cardiac catheterization and other contrast-enhanced procedures, or in the status of the patient at the time of the radiographic procedure (outpatient *versus* hospitalized) in regard to determining patients' risk level for CIAKI or implementing preventive measures (6,16–18). Additionally, it remains unclear whether the morbidity and mortality that have been associated with CIAKI among hospitalized patients are present among outpatients.

A large proportion of patients who receive intravascular iodinated contrast do so when undergoing outpatient computed tomography. The routine assessment of risk status and implementation of preventive interventions, such as IV fluid, are considerably more difficult in patients who undergo elective computed tomography than coronary angiography. The practical and fiscal challenges to systematically administering preprocedure and postprocedure IV fluid to "at risk" patients are substantial, particularly in the outpatient setting. However, to determine the most effective and practical approach to identifying patients at increased risk for CIAKI following computed

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tomography and implementing preventive care to those most likely to derive benefit, greater clarity is needed on the incidence and clinical sequelae of CIAKI in this patient population. The primary aim of this study was to assess the incidence and outcomes of CIAKI following nonemergent computed tomography in the inpatient and outpatient setting.

## Materials and Methods

### Patient Population

This study was approved by the institutional review board of the VA Pittsburgh Healthcare System. As part of a larger, prospective, observational study investigating the prevention of CIAKI in patients undergoing coronary or noncoronary angiography or computed tomography at an academically affiliated VA Healthcare System between February 1, 2005 and July 31, 2006, we conducted this substudy of patients who underwent computed tomography (19). We prospectively identified all subjects scheduled to undergo computed tomography with IV iodinated contrast in either the inpatient or outpatient setting and recorded the most recent serum creatinine (Scr) within the 60 d before the procedure. Using this Scr value, we calculated patients' baseline estimated GFR (eGFR) using the 4-variable Modification of Diet in Renal Disease study equation (20). Patients scheduled to undergo computed tomography with IV contrast at the study VA Healthcare System are recommended to have a baseline Scr measured within the 2 months before the planned procedure in order for radiology personnel to identify patients at increased risk for CIAKI. This allowed us to determine patients' preprocedure level of renal function and to enroll only those at increased risk for CIAKI based on a baseline eGFR of  $<60$  ml/min per  $1.73$  m<sup>2</sup>. We did not enroll patients with end-stage renal disease on chronic dialysis or those unable to provide informed consent based on the need for mechanical ventilation at the time of the procedure. We also excluded subjects undergoing computed tomography for the diagnosis of acute pulmonary embolism or ruptured aortic aneurysm, so we could assess provider use of preventive care for CIAKI, including the use of IV fluids and NAC and the discontinuation of nonsteroidal anti-inflammatory agents (NSAIDs). To limit the study to patients whose primary risk factor for acute kidney injury was the administration of IV contrast, we excluded patients receiving IV vasopressor or inotropic medications and hospitalized patients with a recorded systolic blood pressure  $<90$  mmHg at the time of the procedure, who were at increased risk for ischemia-induced acute kidney injury.

Radiology personnel approached eligible subjects at the time of the procedure to introduce the study. For interested patients, a study coordinator explained the study in detail and obtained informed consent.

### Baseline Data Collection

We collected demographic data from patients and asked about current use of prescribed or over-the-counter NSAIDs other than once-daily aspirin. We asked patients taking NSAIDs if they were instructed to discontinue the medication before the procedure, and if so, whether they complied. The study coordinator also asked patients whether they were instructed to increase their oral fluid intake in advance of the procedure, and if so, whether they did so. We also recorded the type and volume of contrast media administered and treatment location at the time of the procedure (inpatient *versus* outpatient). Patients residing at a nursing facility were considered inpatients. For patients undergoing outpatient procedures, arrangements were made for a Scr to be measured at a VA laboratory 48 to 96 h following the procedure. Although we aimed to have this test performed approximately 48 h following all outpatient procedures, we extended this window to 96 h because VA laboratory facilities are not open on weekends. For inpa-

tients, we ordered a 48-h postprocedure Scr and recorded all postprocedure Scr measurements performed in the hospital.

Using the electronic medical record, we identified all prescription medications and comorbid medical conditions, including diabetes mellitus, congestive heart failure, liver disease, and cerebral, peripheral, and/or coronary vascular disease. This electronic medical record review also included an assessment of the use of periprocedure IV fluid and NAC. Of note, there was no formal protocol for the prevention of CIAKI at our institution at the time of this study.

### Follow-up Data Collection

To evaluate medical outcomes associated with CIAKI, we conducted 30-d medical record reviews and telephone interviews to determine vital status, whether postprocedure dialysis was required, and hospital admissions not including those immediately following the index computed tomography scan. The medical record review was based on a comprehensive assessment of the integrated VA electronic health record that captures all visits, hospitalizations, and procedures at any VA facility nationwide. The review of hospitalizations included an assessment of whether the admission was the result of kidney disease. As a safety precaution, we performed a repeat Scr in all outpatients who manifested a postprocedure rise in Scr  $\geq 25\%$  to ensure that progressive renal failure did not develop.

### Statistical Analyses

Our primary analyses were based on assessing the incidence of CIAKI and the associations of CIAKI with 30-d outcomes in the overall study population, and among subgroups of patients defined by location at the time of the procedure (inpatient *versus* outpatient) and baseline eGFR ( $\leq$  or  $>45$  ml/min per  $1.73$  m<sup>2</sup>). Because there is no consensus on the most valid definition of CIAKI, we evaluated the incidence of this condition using three nonmutually exclusive definitions based on relative increases in Scr from baseline ( $\geq 25\%$ ,  $\geq 50\%$ , and  $\geq 100\%$ ) and three absolute increments in Scr from baseline ( $\geq 0.25$  mg/dl,  $\geq 0.5$  mg/dl, and  $\geq 1.0$  mg/dl). We also assessed the incidence of CIAKI based on the RIFLE criteria, which defines acute kidney injury based on 5 distinct categories: Risk, Injury, Failure, Loss, and End-stage kidney disease. Because we did not collect urine output data, these assessments were based solely on changes in Scr. Among hospitalized patients with multiple postprocedure Scr measurements, the development of CIAKI was determined by the maximal change in Scr within 96 h.

Differences in patient characteristics, use of preventive care, and the incidence of CIAKI between outpatients and inpatients were assessed using *t* test, Fisher exact, and  $\chi^2$  tests, as appropriate. Unadjusted associations of CIAKI with 30-d mortality, need for dialysis, and hospitalization were assessed using the Fisher exact test for each of the definitions of CIAKI. Because of the very low incidence of death, we used exact logistic regression to examine the independent association of CIAKI with 30-d mortality, adjusting for potentially confounding covariates that were found to have univariate associations ( $P \leq 0.10$ ) with this outcome. A two-sided *P* value of  $<0.05$  was considered to represent statistical significance. All analyses were conducted using STATA version 9 (College Station, TX).

## Results

### Patient Characteristics

We identified 1162 patients without end-stage renal disease scheduled to undergo computed tomography with IV contrast who had a baseline eGFR  $<60$  ml/min per  $1.73$  m<sup>2</sup>. A total of 484 patients (42%) were unable to provide consent, refused to

participate, or underwent the procedure on the weekend or at night and were unavailable for recruitment. A total of 254 patients (22%) underwent the procedure without IV contrast, and three underwent emergent procedures or had reduced blood pressure and were excluded (Figure 1). The remaining 421 patients comprised our study population, of whom 294 (70%) were outpatients and 127 (30%) were hospitalized. A total of 326 patients (77%) had their baseline Scr measured within 24 h before the procedure, and 396 patients (94%) had the preprocedure Scr assessment within 7 d before the procedure. The mean age of study patients was 69 yr, 403 (96%) were male, and 172 (41%) had diabetes mellitus. Inpatients were more likely than outpatients to have congestive heart failure and cerebrovascular disease (Table 1).

#### Procedural Characteristics and Use of Preventive Care

The median volume of contrast was 150 ml (range, 10 to 200 ml). Fifteen patients underwent postradiation computed tomography of the pelvis using <100 ml of contrast. Fifty-nine patients (14%) received low osmolal Iohexol (Omnipaque, GE Healthcare, Princeton, NJ), whereas 362 (86%) received iso-osmolal Iodixanol (Visipaque, GE Healthcare). Only 84 patients (20%) received preprocedure IV fluids, 91 (22%) received postprocedure IV fluids, and 70 (17%) received both preprocedure and postprocedure IV fluids. Inpatients were considerably more likely to receive IV fluids than outpatients (Table 2). The most commonly used IV fluid among patients who received this therapy was isotonic sodium chloride (65% of preprocedure use and 64% of postprocedure use). NAC was administered to 73 patients (17%) overall: 48 inpatients (38%) and 25 outpatients (8.5%). Of 40 patients who were receiving NSAIDs at the time of the procedure, none was instructed to discontinue the medication.

Hospitalized patients were considerably more likely to re-

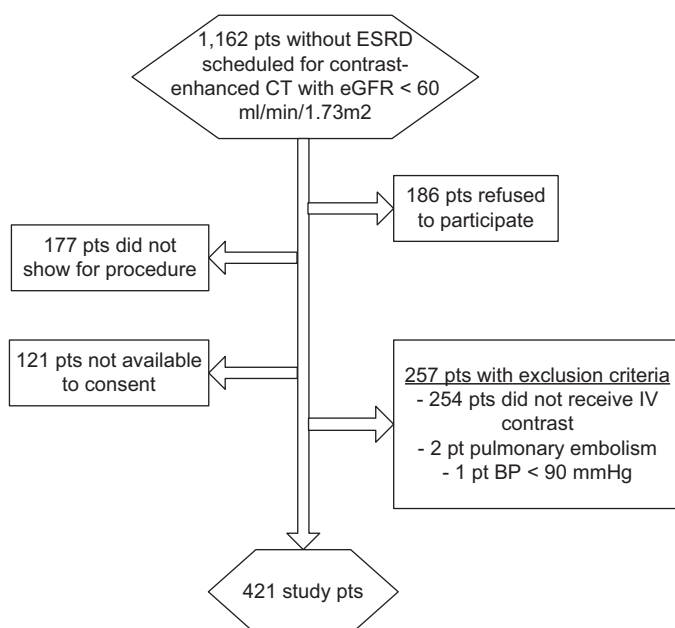


Figure 1. Patient selection.

ceive preprocedure and postprocedure IV fluid (odds ratio = 11.7; 95% confidence interval, 6.2, 22.0) and NAC (odds ratio = 7.1; 95% confidence interval, 4.0, 12.6), whereas lower baseline eGFR was also associated with a greater likelihood of use of these two preventive interventions. The presence of diabetes mellitus or congestive heart failure was not associated with the use of either of these interventions.

#### Incidence and Predictors of CIAKI

A total of 367 patients (87%) had postprocedure Scr measured. The incidence of CIAKI varied from 0% to 6.5% based on relative increases in Scr of  $\geq 100\%$  to  $\geq 25\%$ , respectively, and from 0.3% to 10.9% with absolute increments in Scr of  $\geq 1.0$  mg/dl to 0.25 mg/dl, respectively. Only 2 patients (0.5%) met criteria for the RISK stage of acute kidney injury (increase in Scr times 1.5) using the RIFLE definition. None of the patients met criteria for more advanced RIFLE stages. CIAKI was more common among patients with baseline eGFR  $\leq 45$  ml/min per 1.73 m<sup>2</sup>. Among subjects with eGFR  $> 45$  ml/min per 1.73 m<sup>2</sup>, CIAKI was considerably more common in hospitalized patients (Table 3). All outpatients with a postprocedure rise in Scr  $\geq 25\%$  had a repeat Scr performed, and none developed more advanced renal insufficiency.

Patient and procedural factors associated with the development of CIAKI, based on two commonly used definitions, an increase in Scr  $\geq 25\%$  and an increase  $\geq 0.5$  mg/dl, are depicted in Table 4. Congestive heart failure, baseline Scr  $> 1.5$  mg/dl, and inpatient status were associated with an increased risk of CIAKI ( $P < 0.05$ ). Baseline eGFR  $\leq 45$  ml/min per 1.73 m<sup>2</sup> was associated with increased risk of CIAKI defined by an increase in Scr  $\geq 0.5$  mg/dl. Use of  $> 100$  ml of contrast was associated with increased risk of CIAKI defined by a rise in Scr  $\geq 25\%$ . There was a slight trend toward a lower risk for CIAKI, defined by an increase in Scr  $\geq 25\%$ , with Iodixanol compared with Iohexol (odds ratio = 0.5,  $P = 0.14$ ), although this difference did not meet the level of statistical significance. No difference in risk for CIAKI, defined by a rise in Scr  $\geq 0.5$  mg/dl, was seen between the two contrast agents. The administration of IV fluids and use of NAC were not associated with a decreased incidence of CIAKI, although patients who received these preventive interventions were considerably more likely to be hospitalized at the time of their procedure and to have lower eGFR, making them a much higher risk group.

#### 30-d Outcomes

We collected 30-d outcome data by electronic medical record review for all 421 patients. Postprocedure 30-d telephone interviews were completed in 264 patients (63%), and we were unable to contact 157 patients. Ten patients (2.4%) died by 30-d follow-up, nine of whom underwent computed tomography as inpatients. None of the study patients required postprocedure dialysis. Forty-six patients (10.9%) were hospitalized within 30 d, but not immediately following the procedure. However, none of the hospital admissions was related to kidney disease.

None of the definitions of CIAKI was associated with an increased risk for 30-d mortality in either univariate or multivariable analyses, as the 95% confidence intervals of all

Table 1. Patient demographic and clinical characteristics

Demographics	Overall (n = 421)	Inpatient (n = 127)	Outpatient (n = 294)	P
age (yr)	69 ± 10	70 ± 10	69 ± 10	0.5
male	403 (96)	121 (95)	282 (96)	0.8
white	385 (91)	114 (90)	271 (92)	0.5
black	31 (7)	11 (9)	20 (7)	0.5
Comorbid illnesses				
diabetes mellitus	172 (41)	60 (47)	112 (38)	0.09
liver disease	59 (14)	20 (16)	39 (13)	0.5
congestive heart failure	68 (16)	30 (24)	38 (13)	0.01
peripheral vascular disease	54 (13)	19 (15)	35 (12)	0.4
cerebrovascular disease	45 (11)	23 (18)	22 (7)	<0.01
Baseline renal function				
serum creatinine (mg/dl)	1.4 (1.3, 1.5)	1.4 (1.3, 1.5)	1.4 (1.3, 1.5)	1.0
eGFR (ml/min per 1.73 m <sup>2</sup> )	53 (48, 57)	52 (49, 56)	53 (48, 57)	0.7
eGFR 30–59 ml/min per 1.73 m <sup>2</sup>	421 (100)	127 (100)	294 (100)	1.0
eGFR 15–29 ml/min per 1.73 m <sup>2</sup>	0 (0)	0 (0)	0 (0)	NC
eGFR <15 ml/min per 1.73 m <sup>2</sup>	0 (0)	0 (0)	0 (0)	NC
Preexisting medication use				
nonsteroidal anti-inflammatories	40 (10)	11 (9)	29 (10)	0.9
loop diuretics	101 (24)	36 (28)	65 (22)	0.2
angiotensin converting enzyme inhibitors	161 (38)	42 (33)	119 (40)	0.2
theophylline	2 (0.5)	1 (1.0)	1 (0.3)	0.5

eGFR, estimated glomerular filtration rate; NC, not calculable. Data are n (%), mean ± SD, or median (interquartile range).

Table 2. Use of preventive care

	Overall (n = 421)	Inpatient (n = 127)	Outpatient (n = 294)	P
Intravenous fluid use				
Preprocedure	84 (20)	62 (49)	22 (7)	<0.01
Postprocedure	91 (22)	70 (55)	21 (7)	<0.01
Preprocedure and postprocedure	70 (17)	53 (42)	17 (6)	<0.01
N-acetylcysteine use	73 (17)	48 (38)	25 (9)	<0.01
Discontinuation of non-steroidal anti-inflammatories <sup>a</sup>	0 (0)	0 (0)	(0) 0	—
Instructed to increase oral fluids	74 (18)	33 (26)	41 (14)	<0.01
Complied with increase in oral fluids <sup>b</sup>	59 (80)	28 (82)	31 (76)	0.4

Data are n (%).

<sup>a</sup>n (%) of the 40 study patients taking nonsteroidal anti-inflammatories.

<sup>b</sup>n (%) of patients who were instructed to increase oral fluids.

odds ratios crossed one (Table 5). CIAKI was not associated with a need for dialysis as none of the study participants required renal replacement therapy following the procedure. Similarly, none of the six definitions of CIAKI was associated with an increased risk for hospital admission (data not shown).

## Discussion

In this prospective, observational study of patients undergoing contrast-enhanced computed tomography, CIAKI was not

uncommon in hospitalized patients and those with more advanced baseline kidney impairment. However, CIAKI occurred very infrequently among outpatients with mild baseline kidney disease, even without the administration of IV fluids in most patients. CIAKI was not associated with need for postprocedure dialysis, hospital admission, or 30-d mortality. These observations have important implications for providers ordering and performing computed tomography, and for future clinical trials of CIAKI in patients undergoing this radiographic procedure.

Table 3. Incidence of contrast-induced acute kidney injury

CIAKI definition	Overall (n = 367)	Inpatient (n = 119)	Outpatient (n = 248)	P <sup>b</sup>
All patients				
≥ 25%	24 (6.5)	15 (12.6)	9 (3.6)	0.001
≥ 50% <sup>a</sup>	2 (0.5)	1 (0.8)	1 (0.4)	0.6
≥ 100%	(0) 0	0 (0)	0 (0)	—
≥ 0.25 mg/dl	40 (10.9)	21 (17.6)	19 (7.7)	0.004
≥ 0.5 mg/dl	13 (3.5)	8 (6.7)	5 (2.0)	0.2
≥ 1.0 mg/dl	1 (0.3)	0 (0)	1 (0.4)	0.5
eGFR ≤ 45 ml/min per 1.73 m <sup>2</sup>	n = 51	n = 15	n = 36	
≥ 25%	6 (11.8)	2 (13.3)	4 (11.1)	0.8
≥ 50% <sup>a</sup>	1 (2.0)	0 (0)	1 (2.8)	0.5
≥ 100%	0 (0)	0 (0)	0 (0)	—
≥ 0.25 mg/dl	7 (13.7)	2 (13.3)	5 (13.9)	0.9
≥ 0.5 mg/dl	5 (9.8)	2 (13.3)	3 (8.3)	0.6
≥ 1.0 mg/dl	1 (2.0)	0 (0)	1 (2.8)	0.5
eGFR > 45 ml/min per 1.73 m <sup>2</sup>	n = 316	n = 104	n = 212	
≥ 25%	18 (5.7)	13 (12.5)	5 (2.4)	<0.001
≥ 50% <sup>a</sup>	1 (0.3)	1 (1)	0 (0)	0.2
≥ 100%	0 (0)	0 (0)	0 (0)	—
≥ 0.25 mg/dl	33 (10.4)	19 (18.3)	14 (6.6)	0.001
≥ 0.5 mg/dl	8 (2.5)	6 (5.7)	2 (0.9)	0.01
≥ 1.0 mg/dl	0 (0)	0 (0)	0 (0)	—

eGFR, estimated glomerular filtration rate; —, not applicable. Data are n (%).

<sup>a</sup>The 2 patients meeting this definition of CIAKI also met criteria for RISK category of acute kidney injury as defined by RIFLE criteria.

<sup>b</sup>Comparison of CIAKI between inpatients and outpatients.

Table 4. Associations of patient and procedural factors with the development of CIAKI

Patient factor	Odds of CIAKI (↑ Scr ≥ 25%)	Odds of CIAKI (↑ Scr ≥ 0.5 mg/dl)
Age >65 yr	1.0 (0.4,2.4)	1.1 (0.3,3.7)
Diabetes mellitus	1.4 (0.6,3.1)	1.2 (0.4,3.5)
Congestive heart failure	2.4 (1.0,5.9)	4.1 (1.3,12.7)
Peripheral vascular disease	2.4 (0.9,6.4)	2.1 (0.5,7.8)
Cerebrovascular disease	1.3 (0.4,4.4)	0.7 (0.1,5.6)
Scr > 1.5 mg/dl	2.5 (1.1,5.9)	5.7 (1.8,17.8)
eGFR ≤ 45 ml/min per 1.73 m <sup>2</sup>	2.1 (0.8,5.6)	4.0 (1.3,12.7)
Hematocrit < 35%	1.8 (0.8,4.3)	2.6 (0.8,7.9)
Inpatient status	3.8 (1.6,9.0)	3.5 (1.1,10.9)
Procedure factors		
Contrast (iso-osmolal)	0.5 (0.2,1.3)	0.9 (0.2,4.4)
Dose contrast > 100 ml	3.3 (1.0,11.5)	2.5 (0.6,11.7)
Preprocedure and postprocedure IV fluid	1.6 (0.6,4.1)	0.8 (0.2,3.8)
N-acetylcysteine use	2.4 (1.9,5.8)	2.0 (0.6,6.7)

Data presented as odds ratios and 95% confidence limits.

The overall incidence of CIAKI in the present study is consistent with that observed in recent clinical trials of patients undergoing computed tomography (21,22). Our results build upon prior studies by describing the very low risk for CIAKI among outpatients with mild kidney disease. These findings are particularly noteworthy considering that preprocedure and/or postprocedure IV fluids were not administered to most outpatients. Only 3.8% of our patients who underwent outpatient procedures with a baseline eGFR >45 ml/min per 1.73 m<sup>2</sup> received preprocedure and postprocedure IV fluid, yet less than 2.5% developed CIAKI. There are significant challenges to the routine use of intravascular volume expansion in patients undergoing contrast-enhanced outpatient computed tomography. Most radiology suites are not adequately equipped or staffed to administer IV fluids, and most insurers do not authorize routine hospital admission for this purpose. However, the very low incidence of CIAKI among outpatients with only mildly reduced eGFR in the current study, less than 4% of whom received preprocedure and postprocedure IV fluids, suggests that the use of intravascular volume expansion may not be routinely necessary in this patient group and may be better reserved for hospitalized patients and outpatients with more advanced baseline renal insufficiency. Indeed, patients who were hospitalized or had lower baseline eGFR levels in our study were more likely to receive preventive interventions for CIAKI and were seemingly more likely to derive benefit from such care.

Table 5. Association of contrast-induced acute kidney injury with mortality

Definition of CIAKI based on $\Delta$ Scr	Unadjusted OR for death <sup>a</sup>	95% CI	Adjusted OR for death <sup>b</sup>	95% CI
$\geq 25\%$	3.8	0.4–20.6	2.2	0.2–14.6
$\geq 50\%$	NC	—	—	—
$\geq 100\%$	NC	—	—	—
$\geq 0.25$ mg/dl	2.1	0.2–11.0	1.7	0.1–10.9
$\geq 0.5$ mg/dl	7.7	0.7–45.9	4.8	0.4–39.5
$\geq 1.0$ mg/dl	NC	—	—	—

OR, odds ratio; CI, confidence interval; NC, not calculable (because of absence of deaths); —, not applicable.

<sup>a</sup>ORs are based on comparisons of patients who did and did not develop CIAKI.

<sup>b</sup>Adjusted for status at time of procedure and cerebrovascular disease.

Although biochemically defined CIAKI was not uncommon in our study population, serious adverse outcomes were rare. None of our patients required dialysis, and there were no associations of CIAKI with need for hospital admission or death at 30 d. In a recent study of 153 patients with chronic kidney disease undergoing contrast-enhanced multidetector computed tomography, CIAKI did not necessitate renal replacement therapy or hospitalization (21). Collectively, our results and the findings of this recent clinical trial suggest that that biochemical evidence of CIAKI in clinically stable patients is not synonymous with clinically significant renal failure.

In addition to providing a scientific basis from which providers will be able to make evidence-based decisions on the risk for CIAKI and need to implement preventive measures, our findings have important research implications. Some past studies have used relatively small increments in Scr as surrogate markers for clinically relevant CIAKI. However, only 2 patients (0.5%) in our study met criteria for the RISK stage of kidney injury using the RIFLE criteria, and none manifested more advanced kidney injury. This suggests that the use of small changes in Scr to estimate sample size requirements, although helping to ensure a sufficient number of primary study “events,” likely results in inadequate power to assess clinically meaningful outcomes (23–28). We conducted *post hoc* analyses to determine the sample size requirements of a clinical trial testing a hypothetical intervention that would reduce the incidence of CIAKI, from 3.5%, which was the incidence in our study using a definition of an increase in Scr  $\geq 0.5$  mg/dl, to 1.75%. Using a type I error of 5% and 80% power, 1393 patients would be needed in each study arm to accurately assess the efficacy of the intervention. A substantially larger study population would be required to detect meaningful differences in outcomes such as death. To date, most studies of CIAKI have enrolled substantially smaller numbers of patients, which has likely confounded efforts to assess the efficacy of preventive interventions for the highest-risk patients. In designing future clinical trials of CIAKI in the setting of computed tomography, investigators should seek to enroll a larger number of high-risk patients and consider incorporating outcomes, such as need for dialysis and/or death in sample size estimates.

There are two potential explanations for the low incidence of CIAKI among outpatients in the present study. First, 254 patients initially scheduled for contrast-enhanced procedures did

not receive IV contrast. The median eGFR of these patients was 9 ml/min per 1.73 m<sup>2</sup> lower than study participants. Although we did not record reasons for the nonuse of IV contrast, perceived risk for CIAKI by radiologists is the likely explanation. Unlike with angiography, computed tomography can be performed without IV contrast. However, for certain indications, diagnostic accuracy decreases without vascular enhancement. Cost-benefit analyses that weigh the short-term advantage of avoiding CIAKI with noncontrast studies with the longer-term risk of failing to diagnose specific conditions will be needed in patients at high risk for CIAKI. Moreover, efforts to delineate the eGFR level below which the risk for clinically consequential CIAKI rises are needed to help inform a practical and feasible approach to implementing preventive care. Our observation that baseline eGFR is a primary driver of the implementation of preventive care underscores the importance of identifying such a threshold. Second, most outpatients (90%) received iso-osmolar Iodixanol, which has been shown in some studies to be less nephrotoxic than low-osmolar Iohexol (29–31). It is plausible that the use of less nephrotoxic contrast media among outpatients with only mildly reduced kidney function provides sufficient protection against CIAKI.

This study has certain limitations. First, our sample size was relatively small; and because many patients had only mildly reduced eGFR and were undergoing nonemergent procedures, our results are not generalizable to higher-risk populations or to patients undergoing sequential procedures with contrast. Second, this was a single-center study, which limits the external validity of our findings. Third, a moderate number of patients were unavailable to provide consent or refused to participate, which reduced the size of evaluable patients. Fourth, there was considerable variability in the timing of postprocedure Scr assessments, and inpatients were more likely to have multiple postprocedure Scr assessments, which could have confounded our assessment of the incidence of CIAKI and comparisons between inpatients and outpatients. However, our evaluation of 30-d outcomes makes up for this limitation by demonstrating that clinically relevant patient outcomes were extremely rare, irrespective of timing of postprocedure Scr measurements. Fifth, although a minority of our patients received IV fluids or NAC, the use of these interventions in approximately 20% of patients, along with the use of iso-osmolar contrast in most subjects, may have contributed to the low incidence of CIAKI.

Sixth, the use of a single preprocedure Scr value to estimate baseline kidney function did not allow us to confirm that abnormal values represented chronic and not acute kidney disease. Lastly, we were unable to determine 30-d outcomes by phone interview in a modest number of patients. However, because all of our patients were receiving care in the VA, which has an integrated electronic medical record that captures patient events at all VA facilities, we likely identified most 30-d outcomes by medical record review alone.

## Conclusions

CIAKI is uncommon following nonemergent, outpatient computed tomography in patients with only mildly impaired baseline kidney function. Clinically significant CIAKI is very rare in this patient setting. These findings will help providers assess the renal safety of iodinated radiocontrast in patients at low to moderate risk for CIAKI who are undergoing computed tomography and should be carefully considered by investigators designing future clinical trials.

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## Disclosures

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See related editorial, “Contrast-Induced Acute Kidney Injury: Is There a Risk after Intravenous Contrast?” on pages 1242–1243.