Clinical Significance of Persistent Global and Focal Computed Tomography Nephrograms After Cardiac Catheterization and Their Relationships to Urinary Biomarkers of Kidney Damage and Procedural Factors

Pilot Study

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Objectives: We evaluate the relationships between persistent computed tomography (CT) nephrograms and acute kidney injury after cardiac catheterization (CC). We compare changes in urinary biomarkers kidney injury molecule 1 (KIM-1), cystatin C, and serum creatinine to procedural factors.

Materials and Methods: From 159 eligible patients without renal insufficiency (estimated glomerular filtration rate >60 mL/min), 40 random patients (age range, 42–81 years; mean age, 64 years; 25 men, 15 women) gave written informed consent to undergo unenhanced CT limited to their kidneys 24 hours after CC. Semiquantitative assessment for global nephrograms and quantitative assessment of focal nephrograms in each kidney was performed. Computed tomography attenuation (Hounsfield units) of the renal cortex was measured. Serum creatinine, KIM-1, and cystatin C were measured before and 24 hours after CC.

Results: Robust linear regression showed that both relative changes in KIM-1 and cystatin C had positive relationships with kidney CT attenuation ($P = 0.012$ and 0.002, respectively). Spearman rank correlation coefficient showed that both absolute changes and relative changes in KIM-1 and cystatin C had positive correlations with global nephrogram grades ($P = 0.025$ and 0.040, respectively, for KIM-1; $P = 0.013$ and 0.019, respectively, for cystatin C).

Conclusions: Global nephrograms on unenhanced CT in patients who have undergone CC are significantly correlated with changes in urinary biomarkers for kidney damage.

Key Words: iodinated contrast media, computed tomography, acute kidney injury, cardiac catheterization, urinary biomarkers, nephrogram

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Acute kidney injury (AKI) after cardiac catheterization (CC) has a reported incidence of 4% to 17%.[1–5] It is most often attributed to intra-arterial (IA) contrast medium (CM) use, but more likely, the cause is multifactorial and includes underlying diseases such as chronic kidney disease (CKD), advanced vascular disease, congestive heart failure and diabetes, use of nephrotoxic drugs, and hemodynamic compromise.[6–11] The current standard measurement to identify patients with postcontrast AKI is serum creatinine (SCr) mainly because it is easy to measure, relatively inexpensive, and widely available. However, it is well known that SCr is insensitive during acute changes in kidney function. Even though a decrease in glomerular filtration rate (GFR) can occur immediately, it may take 48 to 72 hours after the decrease in GFR before SCr rises sufficiently to meet a definition of AKI.[12] It is crucial to detect AKI after CC in a timely manner due to its increased risk of in-hospital mortality and poor long-term survival.[3,5,13] Because patients are typically discharged 24 to 48 hours after CC, there needs to be an earlier and a more sensitive marker of AKI to prevent kidney damage from worsening and to facilitate discharge planning.

Persistent nephrograms on unenhanced computed tomography (CT) scans are often encountered, with a reported incidence of 45% to 62% after IA and 34% after intravenous CM procedures.[2,14–23] Global "sentinel" and focal "spotted" nephrograms have been described. Some studies have hypothesized that persistent nephrograms may be related to AKI, but the poor sensitivity of SCr may account for the lack of a consistent association between these 2 entities.

In the last decade, several serum and urinary biomarkers have been identified for early detection of AKI. Two of the urinary biomarkers are kidney injury molecule 1 (KIM-1) and cystatin C. KIM-1 is a transmembranous glycoprotein that normally has baseline negligible levels in the urine of individuals with normal kidney function, but after ischemic or toxic injury has very elevated levels in the urine derived from injured proximal tubular epithelial cells.[24] Cystatin C is a nonglycosylated proteinase inhibitor that is also expressed in high levels after AKI as a result of a decrease in normal proximal tubule reabsorption of filtered cystatin C.[25] Both of these biomarkers have been shown in studies to be capable of early detection of AKI before there are significant increases in SCr.[12,24–27]

The relationship between persistent CT nephrograms in patients who have undergone a prior intravascular CM procedure and urinary biomarkers of AKI may be important in establishing whether persistent nephrograms are in fact associated with AKI. Therefore, the purpose of this pilot study was to evaluate a possible link between persistent and quantifiable CT nephrograms after CC and changes in KIM-1, cystatin C, SCr, and procedural factors.

MATERIALS AND METHODS

This single-institution prospective study was approved by our institutional review board and carried out in compliance with the Health

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Study Population

From March 2013 to May 2014, 159 patients were recruited at random to undergo a limited CT scan of their kidneys preferably at 24 hours after their scheduled CC but not before 18 or after 30 hours to evaluate for residual CM in their kidneys. Inclusion criteria were age 18 years or older and estimated GFR greater than 60 mL/min per 1.73 m^2. Exclusion criteria were not fulfilling the inclusion criteria, hypersensitivity to iodine-containing compounds, history of AKI requiring dialysis, pregnant or lactating women, and usage of CM for any other radiographic procedure between 72 hours before and 30 hours after the CC. A total of 40 eligible patients completed the study requirements (Fig. 1).

Cardiac Catheterization

Baseline values of complete blood count and chemistry panel were obtained in all patients before and 18 to 30 hours after the CC. Visipaque (iodixanol, 320 mg I/mL; osmolality 290 mOsm/kg and viscosity 11.8 cps at 37°C; GE Healthcare, Princeton, NJ) was injected IA in either the femoral artery or radial artery. After the procedure, the total CM volume, fluoroscopy time, left ventricular ejection fraction (LVEF), and coronary intervention, if any, were recorded. Outpatients who had only a diagnostic CC were discharged home on the same day when hemodynamically stable. Patients who underwent a coronary intervention stayed in the hospital overnight for observation as per standard protocol.

Unenhanced Dual-Energy CT Scan

Between 18 and 30 hours after the CC, all patients underwent an unenhanced dual-energy CT scan through the kidneys (Somatom-Definition DS; Siemens Healthcare, Knoxville, TN), with tube A at 80 kV and 499 mA, tube B at 140 kV and 118 mA (effective milliamperes of 714 and 168, respectively), and a collimation of 14 × 1.2 mm. Two image sets with 5.0-mm-thick and 1.5-mm-thick sections were reconstructed with H30 (medium smooth) and D37s (dual energy, medium sharp) kernels, respectively. Only the 140-kV image sets were used for image analysis.

CT Image Assessment

The CT images were independently assessed by 3 authors: a fourth year radiology resident, an abdominal imaging radiologist with 25 years of clinical experience, and a genitourinary radiologist with 35 years of clinical experience. Each author assessed for bilateral global nephrograms on a pre-established scale: none, faint, moderate, and marked. They also determined the number of focal nephrograms in each kidney and whether there was vicarious excretion in the gallbladder and/or bowel. After the independent assessment, the authors met together and reviewed all the images. Disagreements were resolved by consensus and the resultant determinations entered into the Statistical Analysis Software software.

One author placed circular regions of interest of at least 0.8 cm^2 on the superior, mid, and inferior portions of each renal cortex to measure attenuation in Hounsfield units (HU). The author was blinded to the nephrogram assessments and clinical parameters. The mean attenuation for each kidney was then calculated. The focal nephrograms were not measured quantitatively because they would be too small for precise statistics due to the large standard deviation of an ensemble of such measurements.

Urinary Biomarker and Acute Kidney Injury Analysis

Urine samples of 25 to 50 mL were collected in all patients before and 18 to 30 hours after the CC. All specimens were frozen immediately after collection in a −80°C freezer. The samples were sent on dry ice overnight to a National Institutes of Health core laboratory.

The Meso Scale Discovery Human Kidney Injury Panel-5 Prototype 7-Plex Assay Kit (catalog number N75CA-1; Meso Scale Discovery, Gaithersburg, MD) was used to measure KIM-1 and cystatin C concentrations in all the urine samples. Good reproducibility of standard duplicates was obtained, with an average signal confidence of variability less than 10%. The assay had picogram/milliliter sensitivity

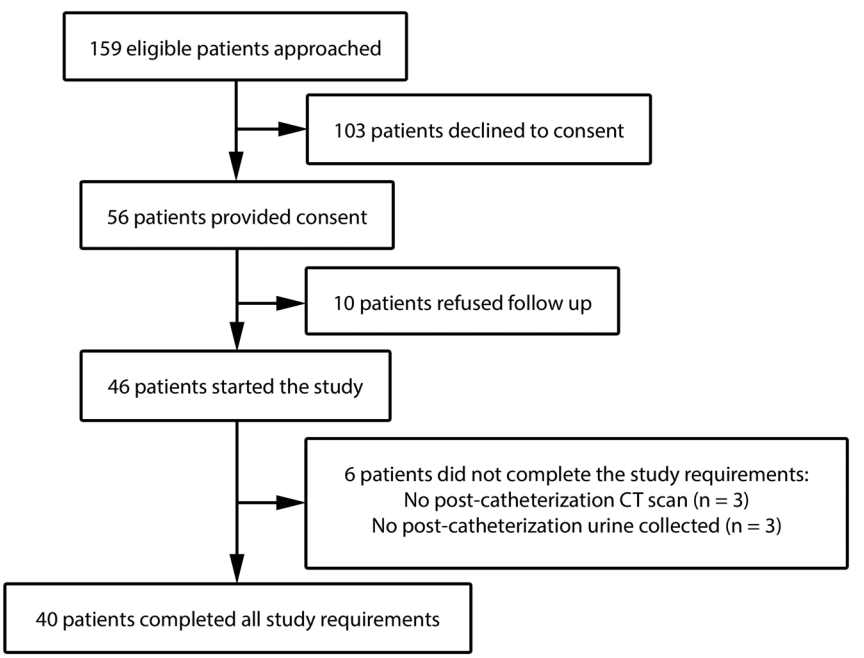

FIGURE 1. Flow chart of study participants.

TABLE 1. Baseline Clinical and Procedural Characteristics

Parameters	Values
Demographics	
Age (range), y	64 ± 10 (42–81)*
Men	25 (62.5%)†
Women	15 (37.5%)
Weight, kg	90.1 ± 19.9 (57–137)
Clinical data	
Baseline SCr, mg/dL	0.90 ± 0.19 (0.55–1.41)
SCr at 24 h postcatheterization	0.88 ± 0.20 (0.56–1.41)
Hyperlipidemia	31 (77.5%)
Hypertension	13 (32.5%)
Diabetes	9 (22.5%)
Procedural data	
Diagnostic catheterization	32 (80%)
Coronary intervention	8 (20%)
Femoral approach	32 (80%)
Radial approach	8 (20%)
LVEF	55.6% ± 10.9% (25.0%–70.0%)
Fluoroscopy time, min	18.8 ± 15.9 (2.3–73.3)
Ventriculograms	33 (82.5%)
Contrast administration	
Contrast volume (iodixanol 320), mL	185.5 ± 104.0 (75.0–500.0)
Iodine load per body weight, g/kg	0.68 ± 0.39 (0.25–2.2)

*Mean ± standard deviation.

†No. patients and percentages in parentheses.

SCr indicates serum creatinine; LVEF, left ventricular ejection fraction.

and covered a broad concentration range, from low picogram/milliliter to 200,000 pg/mL. Urine samples diluted 1:100 yielded good values for cystatin C.

The criteria for AKI defined by the American College of Radiology (ACR) are an increase in SCr by 0.5 mg/dL or 25% or more from baseline value within 3 days after contrast administration.[28]

Statistical Analysis

Statistical analysis was performed with Statistical Analysis Software version 9.4 (SAS Inc, Cary, NC). Spearman rank correlation coefficient was used to evaluate the correlations between each outcome variable (kidney attenuation, bilateral global nephrogram grade, and bilateral total number of focal nephrograms) and each predictor (contrast volume, fluoroscopy time, baseline SCr, and relative change in SCr). Relative change is defined as the absolute change divided by the baseline value. Spearman rank correlation coefficient was also used to evaluate the correlations between the relative change in each urinary biomarker from baseline to after catheterization and each predictor: age, LVEF, baseline SCr, relative change in SCr, iodine load per body weight, and fluoroscopy time. Wilcoxon rank sum test was used to assess whether there was a statistically significant difference in the relative change in each urinary biomarker between groups with and without diabetes, hypertension, hyperlipidemia, and/or anemia. Robust linear regression was used to study the relationship between relative change in each urinary biomarker with kidney attenuation. Spearman rank correlation coefficient was used to evaluate the correlations between absolute change and relative change in each urinary biomarker with global nephrogram grade and bilateral total number of focal nephrograms. A P value less than 0.05 was considered statistically significant. We report the exact P values unless the P value is very small (almost 0), where the P value is less than 0.0001.

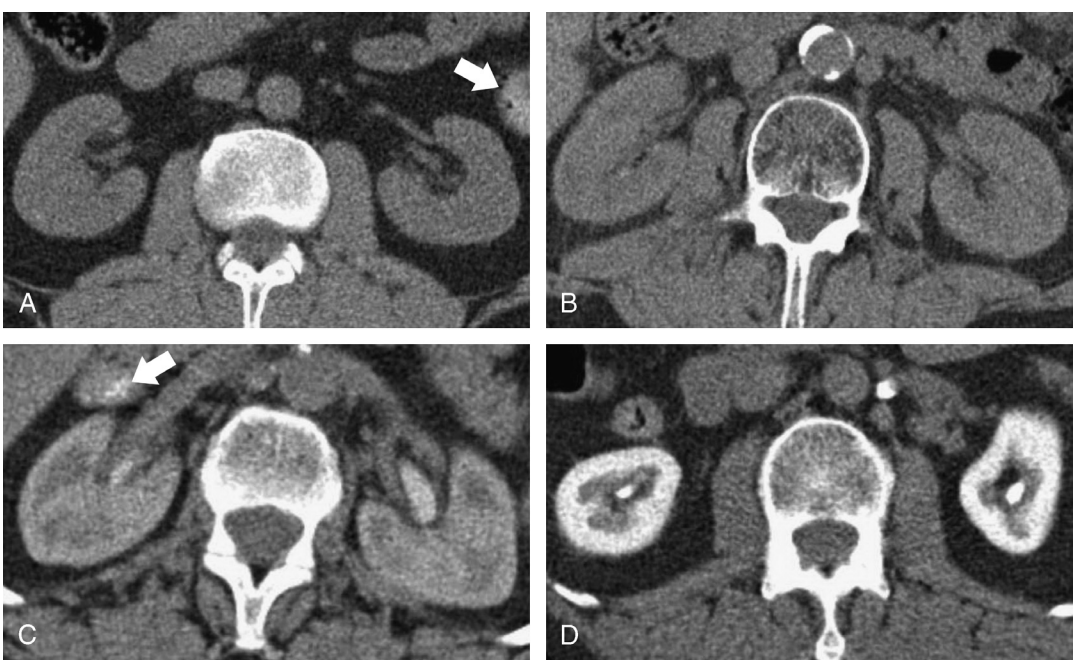

FIGURE 2. Axial unenhanced CT scans through the kidneys of 4 different patients 24 hours after CC. Kidneys were graded on the extent of persistent global nephrogram: (A) none, median cortical attenuation values 35.2 HU and 34.3 HU right and left kidneys, respectively; (B) faint, 64.9 HU and 61.8 HU right and left, respectively; (C) moderate, 91.8 HU and 93.6 HU right and left, respectively; and (D) marked, 156.4 HU and 163.3 HU right and left, respectively. Vicarious excretion of contrast in the small bowel is noted in the figures A and C (arrows).

RESULTS

Patient Demographics and Cardiac Catheterization

The patient demographics and CC details are listed in Table 1. No patients were hemodynamically unstable or experienced clinically significant hypotension (systolic blood pressure less than 80 mm Hg).

Kidney CT Attenuation, Nephrograms, and Procedural Factors

The mean time from CC to CT was 23.4 ± 2.8 hours (18.5–29.3 hours). For the global nephrograms, there was 85% (34/40) agreement before the consensus meeting, and 88.75% (71/80) for the focal nephrogram determinations. The disagreements were all resolved by consensus. Twenty-one patients (52.5%) had abnormal nephrograms. Seven patients (17.5%) had both global and focal nephrograms. Global nephrograms were bilateral and observed in a total of 14 patients (35.0%) (Figs. 2, 3). Ten patients (25.0%) had faint global nephrograms, 1 patient (2.5%) had a moderate global nephrogram, and 3 patients (7.5%) had marked global nephrograms. The mean attenuations were 45.6 ± 5.69 HU (34.1–58.0 HU) for no global nephrograms, 54.6 ± 12.6 HU (38.6–83.5 HU) for faint global nephrograms, 95.3 ± 0.02 HU (95.3–95.3 HU) for moderate global nephrograms, and 143 ± 14.9 HU (123–159 HU) for marked global nephrograms. Focal nephrograms were observed in a total of 13 patients (32.5%) (Fig. 4). Four patients (10.0%) had 1 focal nephrogram, 7 patients (17.5%) had 2 focal nephrograms, and 2 patients (5.0%) had 3 focal nephrograms. Twenty-four patients (60%) had vicarious excretion of contrast in the gallbladder and/or bowel. There was no significant correlation between kidney attenuation and time from catheterization to CT.

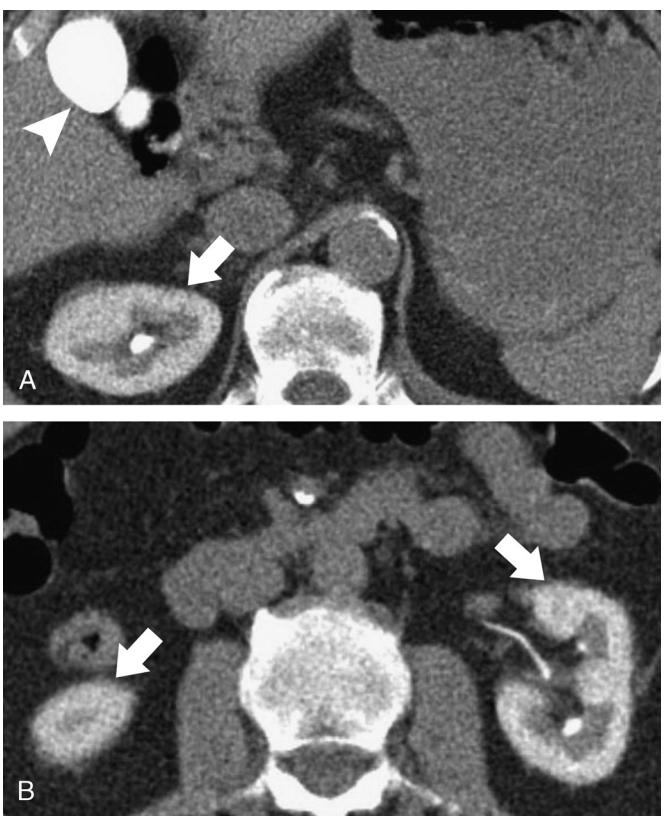

FIGURE 3. Axial unenhanced CT scan in an 80-year-old man 24 hours after angioplasties and placement of 3 stents. The procedure required 500 mL (2.2 g I/kg) of iodixanol 320 and 73.3 minutes of fluoroscopy time. Bilateral global nephrograms with corticomedullary distinction. Right kidney (A, arrow) with cortical attenuation of 150.17 HU and vicarious excretion into the gallbladder lumen (arrowhead). Lower abdominal image (B) through lower pole of right kidney and mid region of left kidney (arrows). Left kidney cortical attenuation of 158.8 HU.

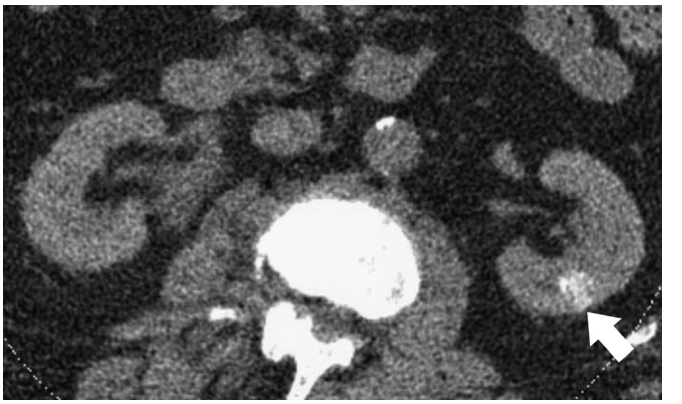

FIGURE 4. Axial unenhanced CT scan through the kidneys 24 hours after CC in a 72-year-old man shows bilateral faint global nephrograms with a focal nephrogram in the left kidney (arrow). This patient had 2 angioplasties and 2 stents, 240 mL (0.92 g I/kg), of iodixanol 320 requiring 21.7 minutes of fluoroscopy time.

Spearman rank correlation coefficient showed that the kidney attenuation and global nephrogram grades had significant positive correlations with contrast volume and fluoroscopy time (Table 2). However, bilateral total number of focal nephrograms had no significant correlation with contrast volume or fluoroscopy time (Table 2). Neither global nephrogram grade nor bilateral total number of focal nephrograms had significant correlations with baseline or relative change in SCr. Bilateral global nephrograms had a higher association ($P = 0.034$) with the femoral than the radial approach. There was no significant difference ($P = 0.37$) between the femoral versus the radial approaches for the occurrence of focal nephrograms.

Urinary Biomarkers and Acute Kidney Injury

The mean ± SD SCr was 0.90 ± 0.19 mg/dL (0.55–1.41 mg/dL) at baseline and 0.88 ± 0.20 mg/dL (0.56–1.41 mg/dL) after CC.

TABLE 2. Spearman Rank Correlation Coefficient for Kidney CT Attenuation (HU), Global Nephrogram Grade, and Bilateral Total Number of Focal Nephrograms Versus Procedural Factors

Characteristic	Measure	Contrast Volume	Fluoroscopy Time
Left kidney CT attenuation	ρ	0.736	0.599
	P	<0.0001	<0.0001
Right kidney CT attenuation	ρ	0.618	0.582
	P	<0.0001	<0.0001
Average of LK/RK CT attenuation	ρ	0.684	0.601
	P	<0.0001	<0.0001
Global nephrogram grade	ρ	0.355	0.529
	P	0.025	0.0004
Bilateral total no. focal nephrograms	ρ	0.002	0.063
	P	0.988	0.698

CT indicates computed tomography; HU, Hounsfield units; LK/RK, left kidney/right kidney.

TABLE 3. Summary Statistics of KIM-1 and Cystatin C

Characteristic	KIM-1	Cystatin C
Baseline, ng/mL	1.09 ± 2.17	96.9 ± 145
Postcatheterization, ng/mL	0.753 ± 1.09	55.5 ± 45.5
Absolute change, ng/mL	−0.337 ± 1.12	−41.5 ± 132
Relative change	0.872 ± 2.18	1.63 ± 6.57
No. patients with +change	17	12
Percent	42.5%	30.0%
Absolute change, ng/mL	0.830 ± 1.01	52.7 ± 43.6
Relative change	4.80 ± 7.88	6.71 ± 10.6
No. patients with −change	23	28
Percent	57.5%	70.0%
Absolute change, ng/mL	−1.20 ± 2.42	−81.8 ± 136
Relative change	−0.707 ± 0.252	−0.551 ± 0.285

KIM-1 indicates kidney injury molecule 1.

None of the patients met the ACR criteria for AKI based on changes in SCr.

The mean time from CC to urine collection for biomarker analysis was 22.6 ± 2.5 hours (18.5–28.2 hours). The summary statistics for the urinary biomarkers KIM-1 and cystatin C is listed in Table 3. There was wide interpatient variability in the urinary biomarker baseline and postcatheterization levels, as well as absolute change and relative change in those levels.

Spearman rank correlation coefficient showed that both relative changes in KIM-1 and cystatin C had significant negative correlations with LVEF ($\rho = -0.35$ [$P = 0.028$] and −0.40 [$P = 0.011$], respectively, both $P < 0.05$). However, neither relative change in KIM-1 nor cystatin C had any significant correlation with age, baseline, or relative change in SCr, iodine load per body weight, or fluoroscopy time. Wilcoxon rank sum test did not show a significant difference in relative change in KIM-1 or cystatin C between groups with and without diabetes, hypertension, hyperlipidemia, or anemia.

Robust linear regression showed that both relative changes in KIM-1 and cystatin C had significant positive relationships with kidney attenuation (β [standard error] = 0.013 [0.005], $P = 0.012$ for KIM-1; 0.577 [0.352], $P = 0.002$ for cystatin C). Spearman rank correlation coefficient also confirmed a significant positive correlation between kidney attenuation and relative change in cystatin C ($\rho = 0.568$, $P = 0.0001$), but did not show a significant correlation between kidney attenuation and relative change in KIM-1.

Spearman rank correlation coefficient showed that both absolute changes and relative changes in KIM-1 and cystatin C had significant positive correlations with global nephrogram grades (Table 4, Fig. 5). Table 5 shows that in general, as the global nephrogram grade increases, the mean change in urinary biomarker from baseline to postcatheterization also increases. The global moderate nephrogram group did not follow this trend due to the fact that there was only 1 patient in that group.

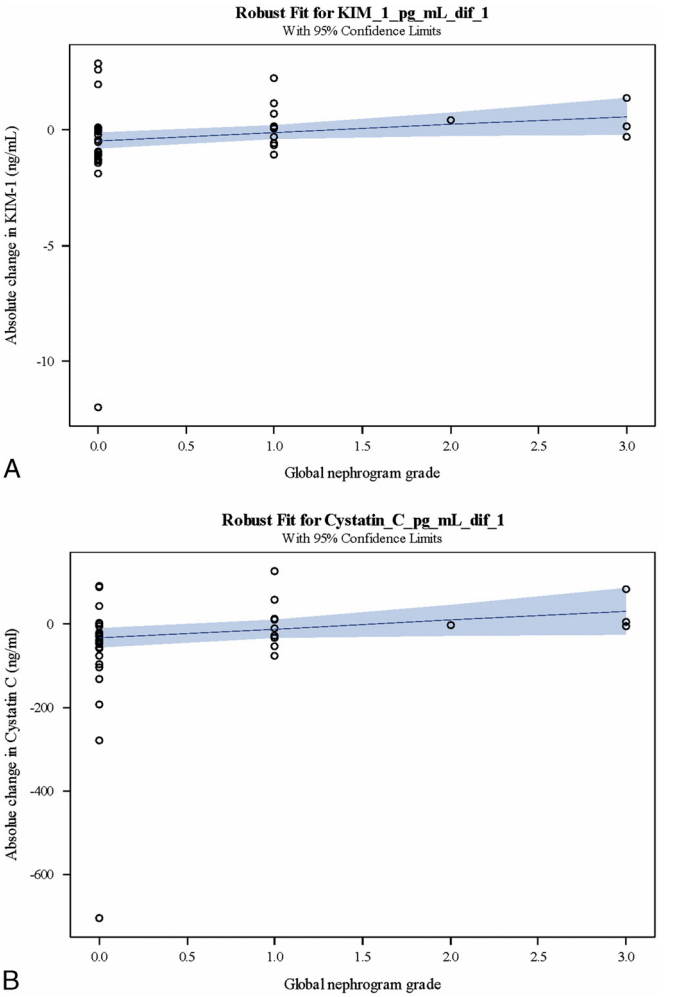

FIGURE 5. A, Scatter plot and robust regression line for absolute change in KIM-1 versus global nephrogram grade that is treated as a continuous predictor (β [standard error] = 0.3473 [0.1537]; $P = 0.0238$). B, Scatter plot and robust regression line for absolute change in cystatin C versus global nephrogram grade that is treated as a continuous predictor (β [standard error] = 20.718 [10.9326]; $P = 0.0581$). Figure 5 can be viewed online in color at www.investigativeradiology.com.

TABLE 4. Spearman Rank Correlation Coefficient for Absolute Changes and Relative Changes in Urinary Biomarkers (in pg/mL) Versus Global Nephrogram Scale and Bilateral Total Number of Focal Nephrograms

		KIM-1 Change		Cystatin C Change	
Characteristic	Measure	Absolute	Relative	Absolute	Relative
Global nephrogram grade	ρ	0.354	0.325	0.390	0.369
	P	0.025	0.040	0.013	0.019
Bilateral total no. focal nephrograms	ρ	−0.283	−0.257	0.028	0.013
	P	0.077	0.109	0.866	0.935

KIM-1 indicates kidney injury molecule 1.

TABLE 5. Global Nephrogram Grade and Change in Urinary Biomarkers

Grade	No. Patients	%	Mean ± SD Change in KIM-1, ng/mL	Mean ± SD Change in Cystatin C, ng/mL
None	26	65.0%	−0.653 ± 2.59	−67.8 ± 153
Faint	10	25.0%	0.181 ± 0.975	2.29 ± 58.2
Moderate	1	2.5%	0.421 ± N/A	−1.50 ± N/A
Marked	3	7.5%	0.413 ± 0.858	28.0 ± 49.4

KIM-1 indicates kidney injury molecule 1; N/A, not applicable.

Neither relative change in KIM-1 nor cystatin C had any significant correlation with bilateral total number of focal nephrograms (Table 4).

DISCUSSION

Persistent nephrograms on unenhanced CT scans performed 24 hours after CC were encountered at a high rate of 53% in our study patients, similar to prior studies.[2,8,18,23] Our pilot study is, to our knowledge, the first attempt to determine whether there is a correlation between persistent CT nephrographic density grading in patients who have undergone an IA contrast procedure, and urinary biomarkers of kidney injury. We found that the relative changes in KIM-1 and cystatin C each had a significant positive correlation with the global nephrogram grade. Although none of our patients met the ACR criteria for postcontrast AKI, these results imply that global nephrograms may represent early kidney damage. There has been increasing awareness of biomarker-positive, SCr-negative AKI.[29,30] Such a pattern is associated with an increase in adverse event rates compared with biomarker-negative, SCr-negative patients. There was no correlation between global nephrograms and baseline or relative changes in SCr from baseline to 24 hours after CC, which supports how insensitive SCr can be as a marker for early kidney damage.

We found that there was no significant correlation between the urinary biomarkers KIM-1 and cystatin C and the bilateral total number of focal nephrograms. Previous studies have speculated that these focal nephrograms represent segmental areas of ischemia caused by blood clots that form around the catheter or cholesterol plaques that are dislodged by the catheter, which lead to emboli in the peripheral vessels, a decrease in glomerular filtration, and CM stagnation in the tubular system.[2,8,18,23] Even though these nephrograms represent foci of kidney ischemia, a possible explanation for why AKI was not reflected in the urinary biomarkers is that renal reserve and compensation is so large.

Our results also show that higher global nephrogram grades and higher kidney attenuation were also associated with higher contrast volumes and longer fluoroscopy times. These results are in line with prior studies.[2,8,18,23] On the other hand, in our study, the bilateral total number of focal nephrograms had no significant correlation with contrast volume or fluoroscopy time. A previous study showed that bilateral total number of focal nephrograms on unenhanced CT performed 24 hours after CC had a significant correlation with fluoroscopy time but not with contrast volume.[8] Perhaps the discrepancy between the bilateral total number of nephrograms and fluoroscopy time is due to the small patient populations in both studies.

We also found a significant positive correlation between the urinary biomarkers and LVEF. Indeed, LVEF has been shown to be an independent predictor of AKI in patients undergoing percutaneous coronary intervention.[31,32] The procedural components of CC, fluoroscopy time, catheter manipulation, and contrast use are interrelated. The linkage between fluoroscopy time and the occurrence of global nephrograms is partly related to the high correlation ($P = 0.815$; $P < 0.0001$; Spearman rank correlation coefficient) with contrast volume. That is, the more difficult or involved is the procedure, the more catheter manipulation is needed, and thus, the more contrast need for guidance. Another possibility is that the greater fluoroscopy time needed to direct catheter placement, the greater the mechanical stimulation of the rich network of sympathetic nerve fibers in the aorta resulting in renal vasoconstriction. Reduced cardiac output leads to reduced renal blood flow, resulting in hypoxia and release of reactive oxygen species. Age, presence of diabetes, hypertension, hyperlipidemia, and anemia were not significantly associated with relative change in either urinary biomarker.

Studies have suggested that persistent global nephrograms are an indicator of AKI. Love et al and Older et al reported that this finding detected by either plain radiography or delayed CT is indicative of postcontrast nephropathy.[15,20] Love et al[15] proposed a cortical attenuation range of 55 to 110 HU at 24 hours to identify patients with subclinical renal impairment and values in excess of 140 HU to be an early indicator of postcontrast nephropathy. On the other hand, Jakobsen et al[33] demonstrated a persistence of the cortical nephrogram by sequentially timed delayed CT scans and postulated that CM retention occurred in the proximal tubular cells, being greater for the nonionic dimer iodixanol compared with nonionic monomers and not being associated with AKI. The attenuation that we have observed and those reported in other studies are generally much higher than that reported by Jakobsen et al.[18,22,23]

Jost et al[34] compared the kidney retention times of high viscosity iodixanol 320 and low viscosity iopromide 300 in the kidneys of healthy and renally impaired rats. They found significantly increased retention times in rats treated with iodixanol 320. In addition, the transcript levels of KIM-1 and another biomarker heme oxygenase 1 (HO-1) were significantly increased in rats that had prolonged renal retention of iodixanol 320 at 24 hours. They offered a hypothesis that prolonged CM exposure resulted in higher renal toxicity. Our study builds upon this previous work by translating animal research to human application. We also evaluated iodixanol 320 as it is the CM that is used during CCs at our institution.

Several studies, mostly in the cardiac and renal literature, have evaluated the usefulness of urinary biomarkers including KIM-1[27]) and cystatin C[12,25–27,35] for early detection of AKI after CC. We are encouraged by the results in this exploratory study because we have as yet to attempt to optimize the timing synchronization between changes in KIM-1, cystatin C, and kidney attenuation either in patients with or without CKD. Given that the normal biologic half-life of CM is 1.5 hours and 94% of the CM is cleared after 6 hours, that is, 4 half-lives, postcatheterization patients could undergo this CT before discharge without any significant interruption in patient flow. We estimate an effective dose of approximately 3.4 mSv for each unenhanced CT scan, which is small compared with that of the CC. In addition, the scan is limited to the kidneys and can be rapidly performed.

In a prior study along similar lines, we utilized the dual-energy technique to quantitate single kidney total iodine content and nephrogram conspicuity at 80 kV, virtual 120 kV, and 140 kV. The lower kilovolts are in the direction of the k-edge of iodine that should improve CT image sensitivity to the retained renal CM.[8] The derived iodine burden that was measured in the global nephrograms correlated well with the Hounsfield unit values determined by the region of interest methodology. In the current study, we found that the semiquantitative visual ratings were adequate at 140 kV in comparison to the prior report. It is likely that correlations between Hounsfield units and visual nephrogram ratings would be greater with scanners employing lower kilovolts.

Our study had several limitations. First, we had a small sample size at a single institution. However, even though this is exploratory, we had relatively high percentages of patients with global and/or focal nephrograms. Despite the many variables associated with the technical and clinical aspects of prospective nonselective CC procedures, we are encouraged that the determination of statistically significant correlations between CT nephrograms and urinary biomarkers establish a promising value for the utilization of CT nephrograms as an early detector of AKI in this clinical setting. Second, we had to collect SCr near 24 hours rather than at 48 to 72 hours because we had limited patient participation otherwise. Because SCr levels can peak 3 to 5 days after contrast administration, it is possible that we have underestimated the incidence of postcontrast AKI in our study. On the other hand, we did not expect a high rate of postcontrast AKI because we excluded patients with CKD. Third, we selected a 24-hour (range, 18–30 hours) post-CC time for the CT scans to assure normal contrast renal clearance, on 1 hand, but not too delayed to miss too many cases on the other hand. Chou et al,[2] in an independent, retrospective study, found a time range for delayed CT nephrograms to be between 2.3 and 150 hours (mean 28 ± 33.6 hours). Future studies will

be needed to better optimize the timing of CT acquisition. We believe that more frequent time intervals would be valuable, but would entail greater radiation exposure. Finally, we did not acquire precatheterization CT scans as baseline, but we derived our subjective nephrogram ratings from previous work where access to this information was available. In addition, no patient was enrolled if they had CM within 72 hours of their CC.

In conclusion, we found that global nephrograms in patients who have undergone CC are significantly correlated with changes in urinary biomarkers for kidney damage. The presence and severity of a global nephrogram may represent a sensitive imaging biomarker of early renal impairment after CC. Other contributing factors to global nephrograms include contrast volume and fluoroscopy time.

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