Radiology

ORIGINAL RESEARCH • PEDIATRIC IMAGING

Risk of Acute Kidney Injury Following Contrast-enhanced CT in a Cohort of 10 407 Children and Adolescents

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Conflicts of interest are listed at the end of this article.

See also the editorial by McDonald in this issue.

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Background: Previous studies have challenged the concept of contrast material–induced acute kidney injury (AKI) in adults; however, limited data exist for children and adolescents.

Purpose: To calculate the incidence and determine the risks of AKI in patients who received intravenous iodinated contrast media for CT.

Materials and Methods: This retrospective study was performed at a children's hospital from January 2008 to January 2018 and included patients aged 0–17 years in whom serum creatinine levels were measured within 48 hours before and after CT with or without contrast media. The incidence of AKI was measured according to the AKI Network guidelines. A subgroup analysis with propensity score matching of cases with control patients was performed. Differences before and after stratification based on estimated glomerular filtration rate (eGFR) were explored. Adjusted risk models were developed using log-binomial generalized estimating equations to estimate relative risk (RR).

Results: From a total of 54 000 CT scans, 19 377 scans from 10 407 patients (median age, 8.5 years; IQR, 3–14; 5869 boys, 4538 girls) were included in the analysis. Incidence rate of AKI for the entire sample was 1.5%; it was 1.4% (123 of 8844) in the group that underwent contrast-enhanced CT and 1.6% (171 of 10 533) in the group that did not ($P = .18$). In the contrast-enhanced CT group, AKI incidence was higher in the group with eGFR of at least 60 mL/min/1.73 m^2 and in the group with eGFR lower than 60 mL/min/1.73 m^2 (1.3% and 8.5%, respectively; $P < .001$) compared with the noncontrast group (0.1% and 2.7%, respectively; $P < .001$). Age was found to be a protective factor against AKI, with an RR of 0.96 (95% CI: 0.94, 0.99; $P = .01$), and contrast media increased risk in the subgroup analysis, with an RR of 2.19 (95% CI: 1.11, 4.35; $P = .02$).

Conclusion: The overall incidence of acute kidney injury after contrast-enhanced CT in children and adolescents was very low, and exposure to contrast media did not increase the risk consistently for acute kidney injury among different groups and analyses.

Contrast-associated acute kidney injury (CA-AKI) and postcontrast acute kidney injury (AKI) are synonymous definitions for any form of AKI occurring within 48 hours of intravascular administration of iodinated contrast media during CT (1–4). Contrast-induced AKI constitutes a subset of CA-AKI that is not only temporally linked to contrast media administration but also suggests causality (4–6). The American College of Radiology considers contrast-induced AKI a rare entity, and published studies have been heavily affected by bias and conflation (4,7). It has been reported that physiologic fluctuations in creatinine level (approximately 0.2–0.4 mg/dL [17.7–14.1 μmol/L]) can be misdiagnosed as CA-AKI (8). In addition, meta-analysis showed that AKI rates are equivalent between patients undergoing contrast-enhanced CT and those undergoing noncontrast CT, independent of the route of contrast media administration or the presence of chronic kidney disease (9).

Studies in adults have raised concern that the risk of CA-AKI is overestimated (7,8), including a 3% higher incidence of AKI in the emergency department in patients not exposed to contrast media versus those who were exposed (10). Propensity score matching studies have found that contrast media does not increase the risk for CA-AKI (11,12); these results have been validated by observational studies and meta-analysis (7,13,14). Similarly, in the pediatric population, McDonald et al found no difference in incidence of CA-AKI between patients who had undergone contrast-enhanced CT and those who had not, but the generalizability of their retrospective findings was limited because of the small sample size of

Abbreviations

AKI = acute kidney injury, AKIN = AKI Network, CA-AKI = contrast material–associated AKI, eGFR = estimated glomerular filtration rate, RR = relative risk, sCr = serum creatinine

Summary

Acute kidney injury in this pediatric sample was lower than previously reported, with an overall incidence of 1.5%.

Key Results

- In this retrospective single-center study, the incidence rate of acute kidney injury (AKI) for the entire sample was 1.5% (294 of 19 377) and was not different between the contrast-enhanced CT group (1.4%, 123 of 8844) and the noncontrast CT group (1.6%, 171 of 10 533; $P = .18$).
- AKI incidence in those with an estimated glomerular filtration rate lower than 60 mL/min/1.73 m^2 who underwent contrast-enhanced CT (8.5%, 10 of 118) was higher than that in those who underwent noncontrast CT (2.7%, 169 of 6238; $P < .001$).
- Age was a protective factor for AKI (relative risk = 0.96; $P = .01$).

2201 patients and the low incidence of AKI of 2.8% (15). Gilligan et al retrospectively compared the incidence rate of CA-AKI in two groups of 925 hospitalized children and found that exposure to contrast media was not associated with increased risk for AKI in patients with normal renal function (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73 m^2) (16). Despite these recent contributions to the literature, limited data on CA-AKI exist for children and adolescents.

The aim of this 10-year retrospective cohort study was to compare the incidence of AKI in patients younger than 18 years who received intravenous iodinated contrast media for CT by comparing it with those who did not and to determine the risks associated with AKI.

Materials and Methods

Patients and Clinical Data Collection

In this institutional review board–approved Health Insurance Portability and Accountability Act–compliant retrospective cohort study, we collected data from an urban academic children's hospital (Children's Hospital of Philadelphia) in the United States from January 2008 to January 2018. Informed consent was waived by the institutional review board. The cohort included all consecutive children and adolescents (age range, 0–17 years) in whom serum creatinine levels were available 48 hours before and after undergoing a CT scan with or without contrast media. Data from patients in both hospitalized and ambulatory settings were included to make the study sample representative of pediatric CT practices.

Race and ethnicity data were also gathered from electronic medical records and then divided into the three most common groups for analysis. Given the low proportion of patients who identified as American Indian, Alaska Native, Asian, Hispanic, or Pacific Islander, we decided to combine them in the category "Other" for statistical analysis (17).

Exclusion criteria were dialysis at the time of the study, an initial serum creatinine level of 2.0 mg/dL (176.8 μmol/L) or higher (already meeting partial criteria for severe AKI) (18), insufficient data on serum creatinine levels, falsely low initial serum creatinine levels below 0.05 mg/dL (4.42 μmol/L) to avoid false-positive cases, and age of 18 or more years at the time of CT scanning (Fig 1).

CT Scanning and Contrast Media Protocol

All studies were performed with pediatric protocols, including weight-based dose-limiting techniques and automatic tube current modulation to limit radiation exposure. CT studies performed at our institution were classified by anatomic section as follows: *(a) head*, including the brain, orbits, face, temporal bones, and sinuses; *(b) neck and spine,* including soft tissues of the neck and the cervical, thoracic, and lumbar spine; *(c) full body*, including chest, abdominal, and pelvic studies; *(d) abdomen and pelvis*, and *(e) extremities*. CT studies were further classified as performed either with or without contrast media. The group that was administered contrast material included patients who received intravenous iohexol (300 mg of iodine per milliliter, Omnipaque; GE Healthcare) at a dose of 2 mL per kilogram of body weight (up to a maximum of 100 mL) according to departmental policy. Also included in this group were patients who received iohexol (350 mg I/mL) for CT angiography, accounting for slightly less than 15% of all contrast-enhanced CT studies during the study period. The third and least common option for contrast media agents is represented by patients with previous adverse reactions to iohexol who received iodixanol (270 mg I/mL, Visipaque; GE Healthcare) and who accounted for less than 1% of contrast-enhanced studies. The contrast media dose is maintained for studies of the brain, neck, thorax, abdomen, and pelvis, as well as for musculoskeletal studies or studies of the extremities.

Outcome Measurements

The primary outcome measurement was the incidence of AKI in patients who received intravenous iodinated contrast media for CT and the risks associated with it compared with those who did not. The definition of AKI was based on changes to creatinine level in all study patients according to the AKI Network (AKIN) definition guidelines (ie, an increase in serum creatinine level ≥0.3 mg/dL [26.5 μmol/L] or ≥50% within 48 hours) (19). Urine output of less than 0.5 mL per kilogram of body weight per hour for more than 6 hours is another independent criterion that can be used to diagnose AKI based on AKIN guidelines; however, we did not include urine output in our analysis, given that available data were incomplete and heterogenous to be able to be used in our statistical analysis. The alternative definition used to detect CA-AKI, contrast-induced nephropathy criteria, was not used in this study, given the higher sensitivity of AKIN (4,20).

Statistical Analyses

Patients who met inclusion criteria were then analyzed in four different groups to account for bias and to enable comparison with prior published studies. The groups were: *(a)* the entire sample, *(b)* paired analysis in patients who underwent both

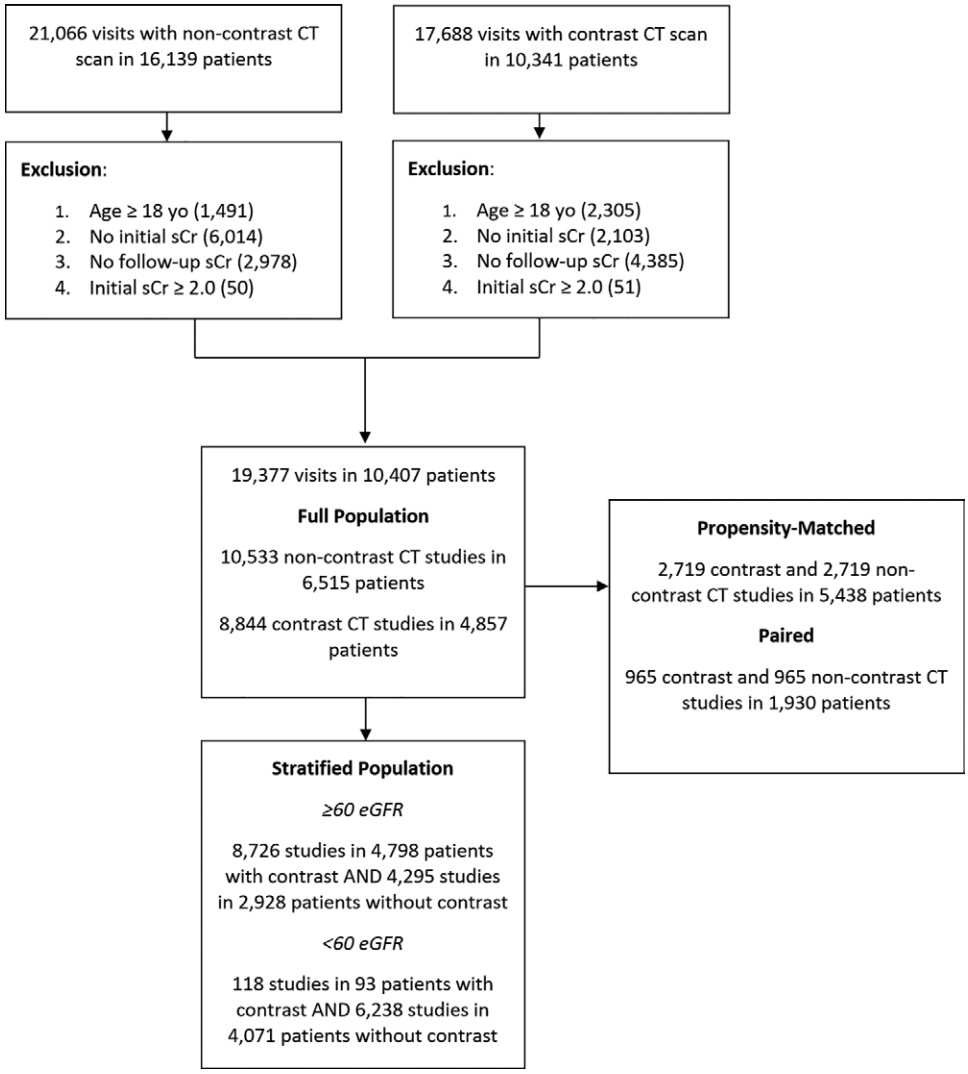

Figure 1: Flowchart shows the process used to select patients. eGFR = estimated glomerular filtration rate, sCr = serum creatinine.

contrast-enhanced and noncontrast CT studies, *(c)* stratified by eGFR into patients with an eGFR of at least 60 mL/min/1.73 m^2 and patients with an eGFR lower than 60 mL/min/1.73 m^2 using the bedside Schwartz formula (eGFR = 0.413 × height/serum creatinine level [measured in milligrams per deciliter]), and *(d)* propensity matched, where a propensity score matched patients who underwent contrast-enhanced CT with patients who underwent noncontrast CT on the basis of age, sex, race, baseline eGFR, and number of scans using a greedy algorithm and a caliper of 0.2 (Fig 1) (21). On the basis of our hypothesis and the findings of previously published studies and assuming a difference in incidence of 1%, an alternative hypothesis of 0.5, α = .05, and 95% power, the calculated sample size was 7674 patients (3837 patients per group).

In the paired and propensity-matched analysis, repeated scans from the same patient were sorted into contrast-enhanced and noncontrast groups, choosing the first scan with an AKI event or the first scan if the patient had no AKI events in that arm, to accurately represent the number of patients with an AKI event. These sorted scans were then patient or propensity matched to obtain a one-to-one pairing between contrast-enhanced and noncontrast scans for the analysis of these groups. Propensity score matching was also considered using an optimal algorithm and a caliper of 100 with propensity score matching using race and sex; these results were very similar to those obtained with other methods, so only one propensity score–matched group is presented. This group is referred to as the propensity-matched group throughout this report.

Data from the four groups mentioned previously were analyzed first to check the balance between the contrast-enhanced CT and noncontrast CT arms of the clinical and demographic characteristics. This analysis used percentages with counts along with the χ^2 test for unpaired variables or the McNemar test for paired association for categorical variables. For continuous variables, because of skewed distributions, median and interquartile range were reported, and differences were evaluated with the Kruskal-Wallis or paired Wilcoxon test (Tables 1, 2).

Table 1: Descriptive Characteristics of the Study Groups

Characteristic	Full Group*			Propensity-matched Group†			Paired Group†		
	Contrast-enhanced Group	Noncontrast Group	*P* Value	Contrast-enhanced Group	Noncontrast Group	*P* Value	Contrast-enhanced Group	Noncontrast Group	*P* Value
No. of patients	4857	6515		2719	2719		965	965	…
No. of scans used in analysis	8844	10 533		2719	2719		965	965	…
Age (y)	10 (5–15)	7 (2–13)	<.001	9 (4–14)	9 (4–14)	.19	7 (4–13)	8 (3–13)	.04
Body mass index	18.3 (16.1–21.8)	17.8 (15.8–20.9)	<.001	18.3 (16.1–21.7)	18.6 (16.3–22.5)	.01	17.6 (15.9–20.5)	17.5 (15.5–20.4)	.15
eGFR‡	122.5 (102.9–146.8)	45.3 (40.9–104)	<.001	114.6 (96.0–135.7)	107.3 (89.3–126.9)	<.001	122 (99.9–148.6)	43.3 (40.5–89.3)	<.001
No. of scans per patient	2 (1–5)	2 (1–4)	<.001	1 (1–2)	1 (1–2)	<.001	1 (1–2)	1 (1–2)	<.001
Female§	3914 (44)	4412 (42)	<.001	1181 (43)	1124 (41)	.11	381 (40)	381 (40)	>.99
Race§									
Black	2284 (26)	3535 (34)	<.001	898 (33)	1173 (43)	<.001	309 (32)	309 (32)	>.99
Other	1638 (18)	1837 (17)	.04	481 (18)	377 (14)	<.001	173 (18)	173 (18)	…
White	4922 (56)	5161 (49)	<.001	1340 (49)	1169 (43)	<.001	483 (50)	483 (50)	…
AKI§	123 (1)	171 (2)	.18	53 (2)	7 (<1)	<.001	38 (4)	15 (2)	.01

Note.—Full, propensity-matched, and paired groups are divided by contrast material exposure. Unless otherwise indicated, data are the median, and data in parentheses are the interquartile range (25th and 75th percentiles). AKI = acute kidney injury, eGFR = estimated glomerular filtration rate.

* *P* value calculated using Kruskal-Wallis test for continuous variables and Pearson χ^2 test for categorical data.

† *Propensity matched* refers to the subgroup of patients who were compared after propensity score matching was applied; *paired* refers to the subgroup of patients compared with themselves (see Materials and Methods). *P* values were calculated using the paired Wilcoxon test for continuous variables, the paired McNemar test for binary categorical variables, and paired symmetry for race.

‡ The eGFR was calculated with the bedside Schwartz equation (0.413 × [height/sCr]) by using pre-CT serum creatinine (sCr) values.

§ Data are number of patients, and data in parentheses are percentages.

Risk models were developed using log binomial generalized estimating equations with an exchangeable covariance structure for scans from the same patient. Relative risks (RRs), their 95% CIs, and *P* values from these models are presented (Table 3).

Statistical significance was indicated by a *P* value less than .05; 95% CIs were calculated, as appropriate. All statistical analyses were performed using SAS, version 9.4 (SAS Institute) (L.B., 9 years of experience).

Results

Patient Characteristics and Incidence of AKI

More than 54 000 CT examinations were performed during the study period, and baseline and follow-up creatinine levels were available for 19 377 encounters in 10 407 unique patients; 8844 CT examinations in 4857 patients included contrast media, and the remaining 10 533 CT examinations in 6515 patients did not (Fig 1). In the contrast-enhanced CT group, median age was 10 years (IQR, 5–15), and 44% were female (n = 3914); in the noncontrast CT group, median age was 7 years (IQR, 2–13), and 42% were female (n = 4412). The number of CT scans by anatomic region with and without contrast media administration was as follows: 1570 and 8534, respectively, for the head; 1361 and 534, respectively, for the neck and spine; 3430 and 1177, respectively, for the full body; 2292 and 141, respectively, for the abdomen and pelvis; and 191 and 147, respectively, for the extremities.

In the full data set, patients who received contrast media were relatively older and had higher eGFR compared with the noncontrast CT group (Table 1, Fig 2). The raw incidence rate of AKI was 1.5% for the entire sample (294 of 19 377); it was 1.4% (123 of 8844) in the contrast-enhanced CT group and 1.6% (171 of 10 533) in the noncontrast CT group (P = .18) (Table 1).

For the paired (same patient) analysis in which patients underwent one scan with contrast media and another without it, patients were equal in all aspects except age and eGFR. At the time the patients received contrast media, they were younger (median, 1 year younger; P = .04) and had a higher eGFR (median, 79 mL/min/1.73 m^2 higher; P < .001) (Table 1). These patients had an AKI incidence of 3.9% (38 of 965) when receiving contrast media compared with 1.6% (15 of 965) when studies were performed without contrast media (P = .01).

For the propensity-matched analysis, AKI incidence was higher in the contrast-enhanced group, demonstrating statistical

Table 2: Descriptive Characteristics of the Study Group Stratified by eGFR with Unadjusted Univariate Analyses

Characteristic	eGFR ≥60 mL/min/1.73 m²			eGFR <60 mL/min/1.73 m²		
	Contrast-enhanced Group	Noncontrast Group	*P* Value*	Contrast-enhanced Group	Noncontrast Goup	*P* Value*
No. of patients	4798	2928	…	93	4071	…
No. of scans used in analysis	8726	4295	…	118	6238	…
Age (y)	10 (5–15)	9 (4–14)	<.001	4 (0.2–13)	6 (2–13)	.01
Body mass index	18.3 (16.2–21.8)	18.2 (16.1–21.5)	.03	18.4 (14.9–21.8)	17.5 (15.6–20.5)	.57
eGFR (mL/min/1.73 m²)†	122.9 (103.3–147.4)	111.5 (94.4–132.2)	<.001	50.6 (41.6–56.3)	41.5 (39.6–43.8)	<.001
No. of scans per patient	2 (1–5)	1 (1–3)	<.001	1 (1–2)	2 (1–3)	<.001
Female	3442 (4)	161 (40)	<.001	48 (41)	2642 (44)	.62
Race						
Black	2247 (26)	1759 (41)	<.001	39 (33)	1777 (29)	.27
Other	1616 (18)	619 (14)	<.001	21 (18)	1214 (19)	.65
White	4863 (56)	1917 (45)	<.001	58 (49)	3247 (52)	.53
AKI	113 (1)	2 (<1)	<.001	10 (8)	169 (3)	<.001

Note.—Unless otherwise indicated, data are median, and data in parentheses are the interquartile range (25th and 75th percentiles). *n* = total number of patients. AKI = acute kidney injury, eGFR = estimated glomerular filtration rate.

* *P* value calculated using Kruskal-Wallis test for continuous variables and Pearson χ^2 test for categorical data.

† The eGFR was calculated with the bedside Schwartz equation (0.413 × [height/sCr]) by using pre-CT serum creatinine (sCr) values.

association between contrast media exposure and AKI (2% vs 0.3%, *P* < .001). The univariable results differed from the paired group in that there was better balance (although still statistically different, *P* = .01) in eGFR and worse balance in race between the contrast-enhanced CT and noncontrast CT groups (Table 1).

Stratified analysis by eGFR (≥60 mL/min/1.73 m², <60 mL/min/1.73 m²) revealed that the group with eGFR less than 60 mL/min/1.73 m² had higher risk for AKI, with an overall incidence of 2.8% (179 of 6356) and 0.9% (115 of 13 021) in those with an eGFR of at least 60 mL/min/1.73 m² (*P* < .001). Encounters in which contrast material was administered had higher incidence of AKI in both the group with eGFR of 60 mL/min/1.73 m² or higher and the group with eGFR lower than 60 mL/min/1.73 m² 1.3% and 8.5%, respectively; *P* < .001) when compared with noncontrast CT encounters (AKI rates of 0.1% and 2.7%, respectively; *P* < .001). However, substantial differences were seen between groups that received contrast media and those that did not. Baseline median eGFR for the contrast-enhanced CT group was 122.5 mL/min/1.73 m² (IQR, 102.9–146.8) versus 45.3 mL/min/1.73 m² (IQR, 40.9–104) for the noncontrast CT group (*P* < .001); and only 93 patients received contrast material when eGFR was lower than 60 mL/min/1.73 m² versus 4798 patients when eGFR was 60 mL/min/1.73 m² or higher (*P* < .001) (Tables 1, 2; Fig 2).

Risk Models for AKI

In the model stratified by eGFR of 60 mL/min/1.73 m² or higher (RR = 25.1; 95% CI: 5.50, 114.8; *P* < .001), paired model (RR = 2.19; 95% CI: 1.11, 4.35; *P* = .02), and propensity-matched model (RR = 7.57; 95% CI: 3.50, 16.4; *P* < 001), contrast media administration was associated with AKI after adjustment for age, body mass index, race, number of scans, and sex. In the full subgroup and the subgroup stratified to eGFR lower than 60 mL/min/1.73 m², contrast media exposure was not associated with AKI (*P* = .39 and *P* = .09, respectively) (Table 3, Fig 3).

In terms of other model covariates, risk models of the entire study sample (full multivariable model) demonstrated differences in age, with older patients having a protective effect against AKI after controlling for the other variables included in the model (RR = 0.96; 95% CI: 0.94, 0.99; *P* = .01). When stratified by eGFR lower than 60 mL/min/1.73 m², results were statistically similar, with age still showing a protective quality (RR = 0.95; 95% CI: 0.91, 0.99; *P* = .02) and eGFR becoming a risk (RR = 1.01; 95% CI: 1.02, 1.09; *P* < .001).

In the stratified analysis, among patients with eGFR of 60 mL/min/1.73 m² or higher, higher body mass index and eGFR values increased the risk for AKI, with RRs of 1.03 (95% CI: 1.01, 1.06; *P* = .02) and 1.01 (95% CI: 1.01, 1.01; *P* < .001), respectively. Conversely, in the paired and propensity-matched models, eGFR did not increase the risk for AKI, with RRs of 1 (95% CI: 0.99, 1.01; *P* = .51) and 1 (95% CI: 0.99, 1.01; *P* = .99), respectively (Table 3; Figs 2, 3).

Discussion

Previous studies have challenged the concept of contrast-induced acute kidney injury (AKI) in adults; however, limited data exist for children and adolescents. In this 10-year retrospective single-center study, AKI was a rare event, with an overall incidence of 1.5% in over 19 000 encounters in patients with baseline serum creatinine levels of less than 2.0 mg/dL (176.8 μmol/L). The incidence of AKI was 1.6% in those who did not receive contrast

Table 3: Adjusted Relative Risks for Developing Acute Kidney Injury

	Full Model		eGFR ≥60 mL/min/1.73 m²		eGFR <60 mL/min/1.73 m²		Propensity-matched Model*		Paired Model†	
Variable	RR	*P* Value	RR	*P* Value	RR	*P* Value	RR	*P* Value	RR	*P* Value
eGFR (mL/min/1.73 m²)‡	0.99 (0.99, 1)	.16	1.01 (1.01, 1.01)	<.001	1.05 (1.02, 1.09)	<.001	1 (0.99, 1.01)	.99	1 (0.99, 1.01)	.51
Contrast enhanced	1.18 (0.81, 1.71)	.39	25.12 (5.5, 114.78)	<.001	2.07 (0.88, 4.86)	.09	7.57 (3.5, 16.37)	<.001	2.19 (1.11, 4.35)	.02
Noncontrast	1 (reference)	…	1 (reference)	…	1 (reference)	…	1 (reference)	…	1 (reference)	…
Age (y)§	0.96 (0.94, 0.99)	.01	1.05 (1, 1.11)	.05	0.95 (0.91, 0.99)	.02	Not estimated	…	Not estimated	…
Body mass index	1 (0.99, 1.01)	.84	1.03 (1.01, 1.06)	.02	0.98 (0.93, 1.03)	.34	Not estimated	…	Not estimated	…
Scans	0.98 (0.94, 1.03)	.4	0.99 (0.94, 1.04)	.58	0.96 (0.87, 1.06)	.44	Not estimated	…	Not estimated	…
Race										
Black	0.88 (0.6, 1.34)	.54	1.13 (0.59, 2.17)	.71	1.05 (0.65, 1.69)	.83	Not estimated	…	Not estimated	…
Other	1 (reference)	…	1 (reference)	…	1 (reference)	…	Not estimated	…	Not estimated	…
White	0.83 (0.57, 1.19)	.3	1.04 (0.56, 1.92)	.9	0.8 (0.51, 1.25)	.32	Not estimated	…	Not estimated	…
Sex										
Male	1.11 (0.84, 1.48)	.47	1.31 (0.8, 2.16)	.28	1.08 (0.76, 1.54)	.65	Not estimated	…	Not estimated	…
Female	1 (reference)	…	1 (reference)	…	1 (reference)	…	Not estimated	…	Not estimated	…

Note.—Unless otherwise indicated, data are relative risk (RR), and data in parentheses are the 95% CI. Relative risks were estimated using log binomial distributed generalized estimating equations with compound symmetry assumed on covariance for scans from the same patient. *P* values and 95% CIs were generated from empirical standard errors and *z* test. eGFR = estimated glomerular filtration rate.

* *Propensity matched* refers to the subgroups that were compared after propensity score matching was applied.

† *Paired* refers to the subgroup compared with themselves (see Materials and Methods).

‡ Age risk was calculated per year.

§ The eGFR was calculated with the bedside Schwartz equation (0.413 × [height/sCr]) by using pre-CT serum creatinine (sCr) values.

media versus 1.4% in those who did. When adjusted for age, body mass index, sex, race, and number of scans, the incidence of AKI was 2% versus 0.3% and 3.9% versus 1.6%, for these propensity-matched and paired models, respectively.

The 1.4% rate of CA-AKI in this population is lower than previously reported in children (15,16), and while the rarity of AKI limits statistical power, this large sample is beneficial in reducing the risk for a type II error. Our findings support recommendations to weigh benefits against the very small but real risk of giving contrast media to children not undergoing dialysis (22,23). While it is likely that in many clinical scenarios such a small risk is outweighed by the need for diagnostic imaging, the consideration remains valid in children, in whom US applications are often the first-line imaging modality regardless of eGFR, and alternative imaging testing with MRI is often available.

In recent years, the CA-AKI controversy has focused on a particular subgroup of patients: those with eGFR lower than 60 mL/min/1.73 m². Two adult studies and one systematic review found no increased risk in giving contrast media to patients with an eGFR higher than 30 mL/min/1.73 m²; in children, however, these findings have been inconclusive or unattainable because of sample size limitations (12,24,25). In the 2020 consensus statement from the American College of Radiology and the National Kidney Foundation regarding the use of intravenous iodinated contrast media in adult patients with kidney disease, the risk of CA-AKI was determined to range from 5% in patients with eGFR of 60 mL/min/1.73 m² or higher to 30% in patients with eGFR of 30 mL/min/1.73 m² or lower (22). We also found a higher rate of CA-AKI in patients with lower eGFR but at a much lower level (1.3% in patients with eGFR ≥60 mL/min/1.73 m² and 8.5% in those with eGFR <60 mL/min/1.73 m²), more than three times lower for both groups.

A recent study by Gilligan et al found that administration of intravenous contrast media does not increase the risk for AKI (odds ratio, 0.91; 95% CI: 0.51, 1.64; *P* = .77) in hospitalized children with stable kidney function when compared with that in patients undergoing US imaging (16). We were not able to validate such findings in our sample, which by design included both hospitalized and outpatient settings, to be able to capture the largest number of patients. McDonald et al (15) also did not find differences in risk of AKI between 1773 pediatric subjects who received contrast media in the emergency

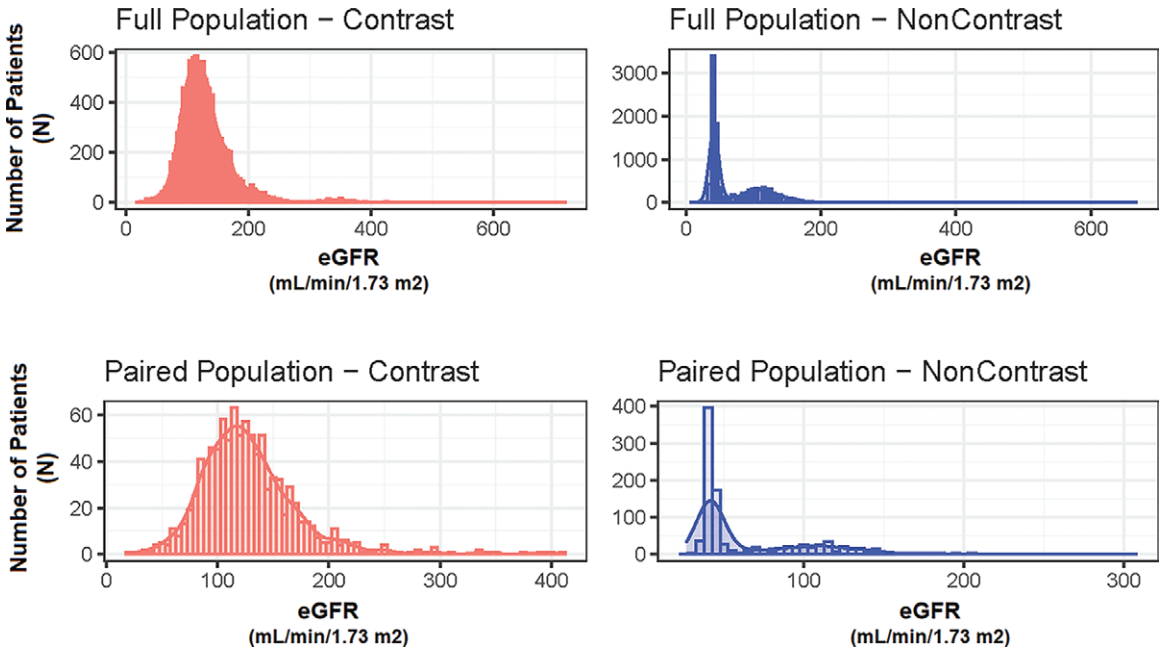

Figure 2: Histograms show estimated glomerular filtration rate (eGFR) distribution for each population studied.

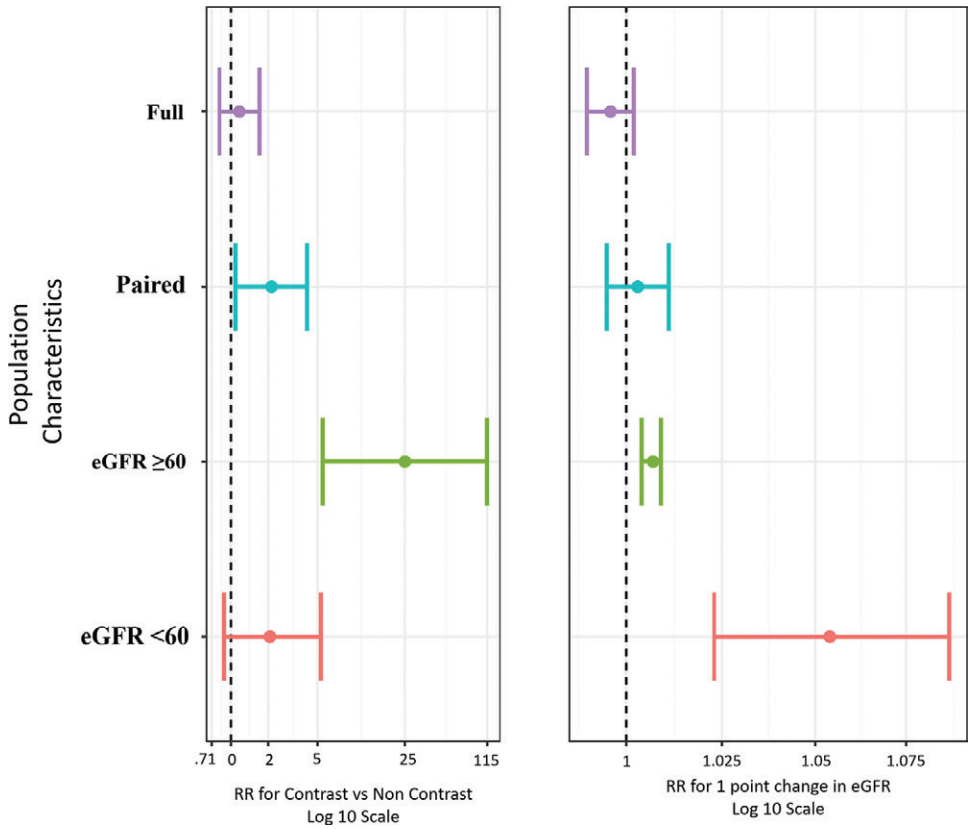

Figure 3: Forest plots for acute kidney injury (AKI) due to contrast-enhanced imaging (left) and estimated glomerular filtration rate (eGFR) (right). Forest plot from the regression model calculating the risk for developing contrast material–associated AKI.

department and inpatient units versus 428 subjects who did not; similar to our study, the unmeasured confounders were a limitation and were present in a relatively small proportion of subjects with a low eGFR at the time of CT.

Our study had several limitations. First, we did not capture confounders—such as preexisting renal disease, presence of comorbidities, and use of nephrotoxic agents, and we included patients with either stable or declining renal function from

the outpatient and inpatient clinical setting. Given similarities among different low- and iso-osmolar contrast agents, it seemed unnecessary to subdivide the groups by contrast media osmolarity (26). Second, CA-AKI in children is a rare event with a large amount of selection bias. Because of preselection bias in our study, children with lower eGFR were less likely to be exposed to iodinated contrast media; hence, the stratified adjusted model lacked power to show differences in risk in these patients with an eGFR lower than 60 mL/min/1.73 m^2, which limits the statistical power and therefore the statistical methods that were applied. Third, we limited our analysis to changes in creatinine values within the 48 hours after contrast media exposure. Cases occurring more than 48 hours after contrast media exposure and other criteria considered by AKIN, such as urine output, were not included. Fourth, for the propensity matching and paired analysis, we did not exclude similar patients who had other unmeasured risks in our database; therefore, a risk for selection bias still exists. We recognize that we might have magnified the incidence of AKI during our paired analysis by selecting those encounters with AKI, regardless of how many other encounters (with or without contrast media) happened before. However, our results must be interpreted in the context of pediatric clinical practice where laboratory data are much less available, preexisting conditions are less common, and rates of CT use are much lower than in adults.

In conclusion, we found that the incidence rate of acute kidney injury (AKI) after contrast-enhanced CT in children and adolescents was lower than in adults. While we found an increased risk for AKI only in a subgroup analysis for exposure to contrast media, clinical importance must be assessed separately. Future studies focused on these subgroups are needed to further evaluate the risks of AKI related to contrast media exposure.

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