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Acute kidney injury following contrast media administration in the septic patient: A retrospective propensity-matched analysis

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ABSTRACT

Purpose: To determine the risk for acute kidney injury (AKI) attributable to intravenous contrast media (CM) administration in septic patients.
Materials and methods: This was a single-center retrospective propensity matched cohort analysis performed in the emergency department (ED) of an academic medical center. All visits for patients ≥18 years who met sepsis diagnostic criteria and had serum creatinine (SCr) measured both on arrival to the ED and again 48 to 72 h later were included. Of 4171 visits, 1464 patients underwent contrast-enhanced CT (CECT), 976 underwent unenhanced CT and 1731 underwent no CT at all.
Results: The primary outcome was incidence of AKI. Logistic regression and between-groups odds ratios with and without propensity-score matching were used to test for an independent association between CM administration and AKI. Incidence of AKI was 7.2%, 9.4% and 9.7% in those who underwent CECT, unenhanced CT and no CT. CM administration was not associated with increased incidence of AKI.
Conclusions: Sepsis is a medical emergency proven to benefit from early diagnosis and rapid initiation of treatment, which is often aided by CECT. Our findings argue against withholding CM for fear of precipitating AKI in potentially septic patients.

1. Background

Contrast-enhanced computed tomography (CECT) plays a central role in the diagnosis and treatment of numerous critical and time-sensitive conditions commonly encountered in emergency and intensive care settings. Over 80 million doses of iodinated contrast media (CM) are administered worldwide each year, placing CM among the most commonly prescribed agents in all of medicine [1,2]. Despite their undisputed clinical value and widespread use, the decision to administer CM is often complicated by a concern for precipitating acute kidney injury (AKI).

Recent studies suggest these concerns may be unwarranted. Multiple large and well-controlled retrospective analyses have found no independent relationship between AKI and CM administration, undermining the long-held belief that CM precipitate AKI [3-8]. While these findings are important and have potential to shift diagnostic and treatment paradigms [9], it is important to note that studies to date have largely focused on defining risk in unselected populations. As a result, uncertainty and concern remain for patient groups known to be at particularly high risk for AKI, including those with sepsis, since less is known about the risk for AKI following CM administration in specific subpopulations.

Sepsis is a leading cause of intensive care unit admission and hospital death worldwide; furthermore, mortality for patients with sepsis who develop AKI is incrementally elevated [10,11]. While the pathophysiology of sepsis itself promotes AKI, preventing secondary kidney injury in septic patients via optimization of hemodynamics and avoidance of iatrogenic renal injury is paramount. Thus, it is important to understand the true contribution of CM to AKI risk in this select patient population. In a recent analysis of 5.9 million U.S. hospitalizations, Wilhelm-Leen et al found that overall incidence of AKI was highest in patients with sepsis and that, in this subgroup specifically, CM administration during hospitalization was associated with an increased incidence of AKI [12].

While the findings above suggest a differential effect of CM on AKI in the setting of sepsis, the findings of this study are limited by its use of administrative diagnoses to define AKI and a database without sufficient granularity to allow for detailed matching analysis or determination of whether CECT was performed before or after development of AKI [12]. In the current study, we sought to clarify the risk for AKI attributable to intravenous (IV) CM administration among patients with sepsis

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using highly detailed, timestamped clinical data and propensity matching analysis. We hypothesized that AKI occurs at higher rates in patients with sepsis who receive IV CM than in those who do not.

2. Methods

2.1. Study design and setting

This was a single-center retrospective cohort study conducted in a large urban academic emergency department (ED) with a mean annual census of 62,179 total visits. All clinical data were abstracted from a relational database that underlies the electronic health record of our institution by an experienced data user as previously described [3].

2.2. Study population

All visits between January 1, 2009 and June 30, 2014 for patients aged 18 years and older who received a CT with or without contrast-enhancement in the ED, had both an initial serum creatinine (SCr) measured in the eight hours prior to CT and a repeat SCr measured 48 to 72 h after the initial CT, and also met sepsis diagnostic criteria during their ED visit were included. During the study period, sepsis was defined according to Sepsis-2 criteria [13]. For study inclusion purposes, patients were determined to have sepsis if: [1] final ED diagnoses included sepsis, severe sepsis or septic shock *or* [2] final ED diagnoses included a specific infection (Supplementary Table 1) *and* two or more systemic inflammatory response syndrome (SIRS) criteria (respiratory rate > 20 breaths/min, temperature > 38 °C or < 36 °C, heart rate > 90 beats/min, or white blood cell count >12,000/mm^3, < 4000/mm^3 or > 10% bands) were met in the ED or a final diagnosis of organ dysfunction was also entered. Diagnoses were determined based on International Classification of Diseases and Clinical Modification, Ninth Edition (ICD-9) codes entered in patients' medical records [14]. To minimize selection bias associated with imaging decisions, we included a second control group of patients who met the same inclusion criteria listed above but did not undergo CT imaging. For these patients, initial SCr measurement could occur at any point during their ED stay.

Exclusion criteria included prior ED visits within 7 days (to limit confounding of pre-existing hospital-acquired AKI), initial SCr <0.4 mg/dL (to minimize inclusion of random laboratory error as cases of AKI), or >4.0 mg/dL (already meeting partial criteria for severe AKI), insufficient SCr data, a history of dialysis, or another CT scan performed within 72 h. CT scans were classified as CECT or unenhanced CT. Consecutive CT acquisitions at different anatomic locations within the same ED visit were treated as a single-scan event and those performed with and without CM were treated as a single CECT. The Johns Hopkins Institutional Review Board approved this study (IRB00027545).

2.3. Contrast media used

Patients who underwent CECT received 80-120 cc of iohexol or iodixanol intravenously according to institutional protocols, available online at www.ctisus.com/protocols.

2.4. Outcome

The primary outcome variable was incidence of AKI as defined by the Kidney Disease Improving Global Outcomes (KDIGO) SCr-based criteria of an absolute increase of at least 0.3 mg/dL or at least a 1.5 times increase over baseline SCr at 48 to 72 h [15,16].

2.5. Analysis

Dichotomous variables were displayed as percentages, categorical data as relative frequencies (in percentages), and continuous data as medians with interquartile ranges (IQRs). Rates of AKI were calculated as the percentage of visits with the occurrence of AKI. A multivariable logistic regression model was used to ascertain whether, and to what degree, CM administration was associated with incidence of AKI in the entire study population after controlling for demographic variables and medical conditions previously reported to increase risk for developing AKI. The independent variable of interest was administration of IV CM. Control variables included age, sex, race, initial SCr, initial estimated glomerular filtration rate (eGFR, calculated by the Modification of Diet in Renal Disease [MDRD] equation), chronic comorbidities and acute illness severity indicators previously shown to predispose to the development of contrast-associated AKI, and administration of nephrotoxic medications or IV crystalloid fluids in the ED [17,18]. Chronic comorbidities included diabetes mellitus, hypertension, HIV/AIDS, congestive heart failure (CHF), chronic kidney disease (CKD), and history of renal transplantation (all identified by ICD-9 codes). Acute illness severity indicators included hypotension (systolic blood pressure < 80 mmHg), designation by an ED attending physician as a patient requiring critical care, anemia (hematocrit <39% or < 36% for males and females, respectively) and hypoalbuminemia (<3.5 g/dL) during the index ED visit. In addition, the All Patient Refined Diagnosis Related Groups (APRDRG) illness complexity and mortality risk categorization was included to further control for illness severity.

The association between CM and AKI was first assessed using the test of proportions to directly compare rates of AKI in septic patients who underwent CECT with those who underwent unenhanced CT and those who did not receive CM. Ordering clinicians are guided by patient pathology and conditional patient-related factors that may predispose patients to the development of AKI following CM administration. To minimize selection bias inherent to the clinical decision associated with administration of CM, we employed propensity-score matching. Variables included in the match were based on their strong relationship to both placement in the treatment group and outcome and were similar to those used in other retrospective studies of AKI [3-6]. Patients in the CECT and non-CECT groups were matched based on gender, age, race, initial SCr, chronic comorbidities (diabetes mellitus, CHF, CKD), whether the patient was designated as requiring critical care, and APRDRG as a measure of illness severity. For propensity score matching, we calculated the average treatment effect using logistic regression assuming a nearest neighbor of one, a caliper of 0.1, and sampling with replacement. A sensitivity analysis examined different caliper restrictions, number of nearest neighbors, and sampling strategies. All comparisons were made for the entire study population and for subgroups stratified by estimated eGFR (which takes account of race and gender based on initial SCr) and by anatomic site of infection (classified by two physicians (JSH and NAJ) based on ICD-9 codes). We re-ran the matching process comparing CT patients with and without contrast (excluding the non-CT patients). Results were presented as average treatment for the treated (ATT) and odds ratios were calculated by logistic regression using the matched sample. All analyses, including propensity score matching, were done in Stata version 14.1 (StataCorp LP, College Station, TX).

3. Results

During the study period, there were 355,690 ED visits by 169,842 patients, of which 4171 visits met all inclusion and no exclusion criteria (Fig. 1). A CT was performed during 2440 visits and 60% of all CT studies were enhanced by IV CM administration (Table 1). The three patient groups (CECT, unenhanced CT, and non-CT) were demographically similar although patients who underwent unenhanced CT were slightly older (Table 1). Similarly, mean initial SCr was lowest in the CECT group at 0.9 mg/dL and highest in the unenhanced CT group at 1.2 mg/dL. Patients who underwent CECT were less likely to have diabetes mellitus, hypertension, congestive heart failure, HIV/AIDS, and chronic kidney disease than those who underwent unenhanced CT; those who had no CT at all were least likely to have any of these comorbidities. Similarly, acute illness severity markers were higher in patients

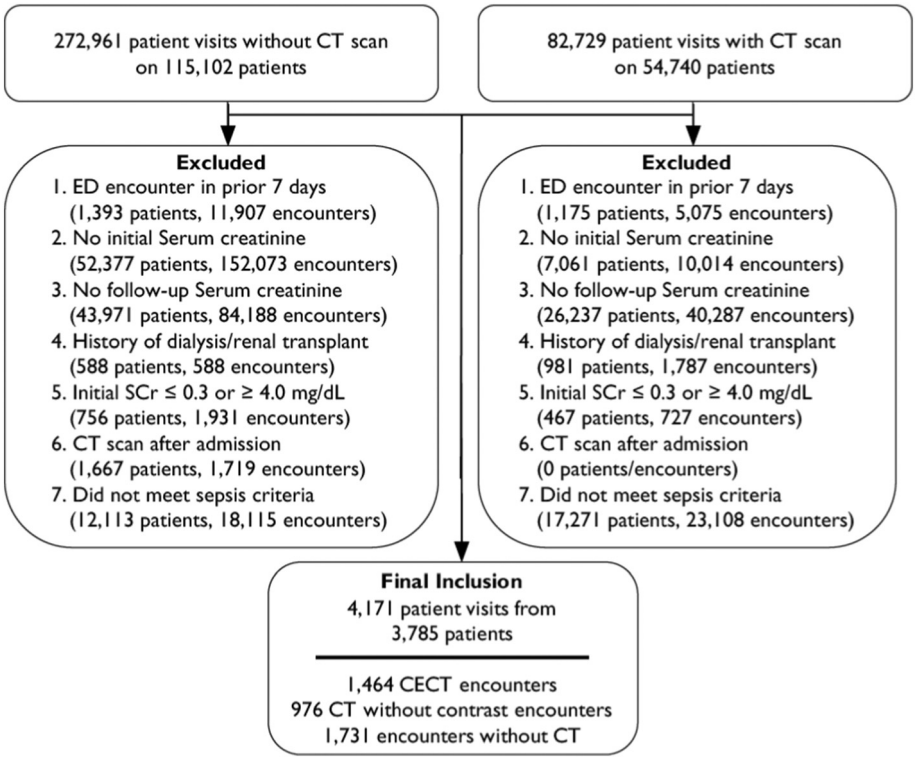

Fig. 1. Flowchart for inclusion and exclusion criteria.

who underwent unenhanced CT than in both the CECT and no CT groups (Table 1).

Incidence of AKI was 7.2% (106/1464), 9.4% (92/976) and 9.7% (168/1731) in the CECT, unenhanced CT, and non-CT groups respectively. Multivariable logistic regression modeling revealed no independent association between CM administration and AKI (Table 2). This was true when performed with all septic patients (OR = 0.93; 95% CI: 0.71–1.20) and the subset who underwent CT (OR = 1.18; 95% CI: 0.83–1.66). Factors most strongly associated with the development of AKI were a pre-existing diagnosis of CHF and a higher severity APRDRG-Mortality Risk score. Administration of IV crystalloid fluid was associated with a decreased likelihood of AKI in all patients (Table 2).

Under direct comparison, CM administration was associated with a decreased risk for developing AKI when compared with patients who did not receive contrast (OR = 0.73; 95% CI 0.58–0.93) but not when comparing those who underwent enhanced versus unenhanced CT (OR = 0.75; 95% CI 0.56–1.00) (Table 3). The propensity score analysis generated fairly balanced populations (Supplementary Table 2 and Supplementary Fig. 1) but found no effect of CM administration on AKI (ATT = −0.02; 95% CI -0.04–0.01 comparing CECT patients to all other patients and ATT = 0.01; 95% CI -0.02–0.03 comparing CECT patients to unenhanced CT patients), and the matched odds-ratios were similarly not significant (OR = 1.08; 95% CI 0.60–1.94 and OR = 1.53; 95% CI 0.83–2.80 respectively). No significant difference was observed in any subgroup stratified by baseline eGFR, including those with the lowest renal function (Table 3). Similar results were observed for subgroup analyses based on anatomic site of infection. The only difference observed in this analysis was a lower risk of AKI associated with CECT as compared with unenhanced CT (OR = 0.24; 95% CI 0.08–0.72) in patients with abdominal infections, an effect that was abrogated after propensity-matching analysis (OR = 1.67; 95% CI 0.19–14.85) (Supplementary Table 3).

4. Discussion

To our knowledge, this is the first well-controlled study to assess for interdependence in the relationship between IV CM administration and AKI in septic patients. Our inability to demonstrate such a relationship is consistent with a growing body of literature suggesting CM plays a much less important role in the precipitation of AKI than previously thought. These findings have important implications for the diagnostic evaluation and management of patients with confirmed or suspected sepsis.

Radiocontrast administration has been associated with AKI in medical literature for over sixty years [19]. The earliest research on this topic was performed in a context where CM were more toxic and volumes of administration exceeded those used today. Perhaps more importantly, the vast majority of studies establishing contrast induced nephropathy (CIN) as an entity were performed in the absence of controls who did not receive contrast, and cases of AKI that followed CM administration were assumed to be caused by CM [20]. More recently, numerous controlled studies have failed to support this causal relationship [21-23]. Most, however, have been retrospective and subject to significant selection bias, as clinicians tend to withhold CM in scenarios where risk for AKI is perceived to be high [3,24]. Multiple groups have sought to minimize bias associated with the decision to administer CM via propensity-matching analysis. Each of these recent studies – all performed in large unselected or critical care cohorts – found no increased risk for AKI, dialysis or death following CM administration [3,5,6,8,25,26]. While one study that employed propensity matching did report increased risk for AKI associated with CM exposure in patients with lowest baseline eGFR (below 30 mL/min/1.73 m^2) [4] three others did not, including one that focused on the critically ill [3,5,27]. A single prospective, case-matched study also failed to find any elevated risk for AKI associated with CM administration in the critically ill [28]. Taken together, these data strongly suggest that risk for AKI associated with CM has long been over-estimated and have led some to question the clinical significance of contrast-induced nephropathy altogether [29,30].

Still, there has been little exploration of the relationship between CM and AKI in specific disease states – including sepsis. Sepsis-associated AKI is thought to represent a unique and particularly morbid subset of AKI [31]. More than one in five patients with sepsis and over half with septic shock develop AKI [31-33]. Those who do are more likely to die than patients with non-septic AKI or sepsis alone [34]. The

Table 1
Patient demographics and clinical characteristics.

Characteristics	Contrast-enhanced CT	Unenhanced CT	Non-CT
Number of patient visits (%)	1464 (35.1%)	976 (23.4%)	1731 (41.5%)
Female, %	50% (728)	49% (474)	53% (909)
Age, y	51 (39–62)	58 (46.5–73)	54 (42–66)
Race			
Black or African American	56.4% (826)	59.4% (580)	61.1% (1057)
Other	7.9% (116)	4.6% (45)	5.0% (87)
White or Caucasian	35.7% (522)	36.0% (351)	33.9% (587)
Initial SCr value (IQR), mg/dL	0.9 (0.7–1.1)	1.2 (0.8–1.8)	1 (0.7–1.4)
eGFR (IQR), mL/min per 1.73 m2	98 (75–116)	65 (38–98)	83 (50–111)
Acute illness severity indicators			
ED critical care designation	4% (62)	6% (58)	3% (44)
Hypotension[a]	9% (129)	11% (106)	7% (121)
Anemia[a]	60% (872)	64% (626)	61% (1049)
Hypoalbuminemia[a]	31% (453)	37% (358)	32% (561)
APRDRG-mortality risk			
1	30.9% (452)	14.6% (142)	25.3% (431)
2	30.1% (440)	29.1% (284)	32.8% (558)
3	28.2% (412)	32.6% (318)	30.2% (514)
4	10.9% (159)	23.7% (231)	11.7% (199)
Medications			
Nephrotoxic medication administration[b]	26% (382)	28% (271)	27% (462)
Crystalloid fluid administration	26% (379)	23% (225)	26% (453)
Comorbidities[c]			
Diabetes mellitus	22% (326)	31% (298)	10% (167)
Hypertension	45% (659)	57% (561)	15% (268)
Congestive heart failure	15% (215)	25% (242)	11% (193)
HIV/AIDS	9% (130)	17% (164)	5% (83)
Chronic kidney disease	6% (92)	29% (279)	5% (91)

IQR, Interquartile range; eGFR, estimated glomerular filtration rate.
[a] Based on vital signs and laboratory analyses from the index ED visit. Anemia: hematocrit level < 39% or < 36% for men and women, respectively; hypoalbuminemia (<3.5 g/dL); hypotension (systolic blood pressure < 80 mmHg).
[b] Medications from the following classes: angiotensin-converting enzyme inhibitor, angiotensin-receptor blocker, antimicrobial, loop and thiazide diuretic, nonsteroidal anti-inflammatory, and other.
[c] Based on ICD-9-CM diagnostic codes from index ED visit or previous hospitalizations.

Table 2
Association between contrast media administration and acute kidney injury in septic patients[a].

Characteristics	All patients	CT patients only
IV contrast administration	0.93 (0.71–1.20)	1.18 (0.83–1.66)
Female	1.16 (0.93–1.46)	1.10 (0.81–1.50)
Age	1.00 (0.99–1.00)	1.00 (0.99–1.01)
Race		
Black or African American	Reference	Reference
Other	1.35 (0.84–2.18)	1.53 (0.84–2.79)
White or Caucasian	0.95 (0.74–1.22)	0.94 (0.66–1.33)
Initial SCr value (IQR), mg/dL	1.06 (0.88–1.28)	0.73 (0.55–0.99)
Acute illness severity indicators £		
ED critical care designation	0.75 (0.43–1.30)	0.89 (0.46–1.70)
Hypotension £	0.64 (0.41–0.98)	0.59 (0.33–1.04)
Anemia £	1.17 (0.91–1.50)	1.21 (0.86–1.71)
Hypoalbuminemia £	0.97 (0.76–1.25)	0.86 (0.61–1.22)
APRDRG-mortality risk		
1	Reference	Reference
2	1.94 (1.29–2.92)	1.95 (1.08–3.52)
3	2.58 (1.71–3.89)	3.12 (1.75–5.58)
4	5.49 (3.49–8.65)	7.40 (3.92–13.95)
Medications		
Nephrotoxic medication administration[b]	1.45 (1.06–2.00)	1.47 (0.98–2.21)
Crystalloid fluid administration	0.44 (0.31–0.64)	0.53 (0.34–0.84)
Comorbidities[c]		
Diabetes mellitus	1.30 (0.97–1.74)	1.52 (1.08–2.14)
Hypertension	0.78 (0.60–1.03)	0.94 (0.66–1.34)
Congestive heart failure	2.50 (1.89–3.30)	1.99 (1.39–2.85)
HIV/AIDS	0.98 (0.65–1.47)	1.17 (0.73–1.90)
Chronic kidney disease	1.34 (0.95–1.88)	2.07 (1.35–3.18)
Constant	0.03 (0.02–0.06)	0.03 (0.01–0.06)
N	4140	2438

[a] Results are odds-ratios with 95% confidence intervals in parentheses. Acute kidney injury defined by Kidney Disease Improving Global Outcomes (KDIGO) as an absolute increase 0.3 mg/dL or 1.5 times increase over baseline SCr at 48 to 72 h. £Based on vital signs and laboratory analyses from the index ED visit. Anemia: hematocrit level < 39% or < 36% for men and women, respectively; hypoalbuminemia (<3.5 g/dL); hypotension (systolic blood pressure < 80 mmHg).
[b] Medications from the following classes: angiotensin-converting enzyme inhibitor, angiotensin-receptor blocker, antimicrobial, loop and thiazide diuretic, nonsteroidal anti-inflammatory, and other.
[c] Based on ICD-9-CM diagnostic codes from the index ED visit or previous hospitalizations.

pathophysiology of sepsis-induced AKI is multi-factorial and includes systemic and intra-renal hemodynamic dysregulation, endothelial dysfunction and direct tubular and glomerular damage [10,11]. Sepsis also increases risk for iatrogenic AKI, as bacterial endotoxin and nephrotoxic medications synergistically precipitate renal dysfunction [35]. This synergism, paired with the assumption that CM are nephrotoxic, has led many to avoid CM administration in septic patients. However, CM administration is often needed to confirm sources of infection or exclude alternate etiologies for critical illness in a timely manner, as recommended in international guidelines [36-38]. Based on the data presented here, avoidance of CM in these cases is likely unwarranted.

Our findings differ from those of a recent study that reported higher rates of AKI in septic patients who received CM than in those who did not [12]. These differences are not surprising and may be explained by divergent study designs. While both studies were retrospective and utilized control populations, Wilhelm Leen et al utilized a very large national database that afforded high sample diversity but lacked patient-level detail required to define outcomes by clinical criteria. Cases of sepsis and AKI were identified using administrative diagnosis codes, which are known to be unreliable and have been reported to be missing for three-quarters of patients meeting clinical criteria for AKI [39]. Indeed, incidence of AKI reported in the Wilhelm Leen et al study was 75% lower than the incidence reported by the same group in a study where AKI incidence was calculated from SCr using international consensus criteria [12,40]. Furthermore, Wilhelm Leen et al were unable to define the temporal relationship between CECT and AKI and cases of AKI that existed prior to CM administration were included in their analysis. Finally, propensity score matching – as performed here – was not possible in their study which increased the opportunity for selection bias.

Our study is strengthened by its large sample size and highly granular clinical dataset, use of two control populations and propensity score matching analysis, but it does have important limitations. First, clinical data from a single academic center were used for analysis and results could reflect practice patterns specific to this institution. In addition, the majority of patients examined were hospitalized for two or more days and it is possible cases of AKI in patients who were discharged earlier were missed. The retrospective nature of the study also limits our analysis to events recorded in the electronic health record (EHR). This could have impacted matching and the composition of our cohort, as all ED patients who met sepsis criteria may not have received a formal diagnosis. We attempted to mitigate the latter by also using vital sign and laboratory-based criteria to identify patients with sepsis. Because clinical diagnoses during the study period were made using Sepsis-2 criteria, vital sign and laboratory-based parameters consistent with this diagnostic framework were employed. Sepsis-3 criteria were not utilized because the retrospective nature of this study did not allow

Table 3
Risk of AKI following IV contrast administration.

eGFR (mL/min per 1.73 m^2)	Rate of AKI by KDIGO criteria			Odds-ratios of AKI by KDIGO criteria (95% CI)				Average treatment effect of CECT[a] on AKI by KDIGO criteria (95% CI)	
	CECT	Unenhanced CT	No CT	Contrast vs. No contrast[b]	CECT vs. unenhanced CT[c]	Contrast vs. No contrast (Propensity Score Matched)[b]	CECT vs. unenhanced CT (Propensity Score Matched)[c]	Contrast vs. No contrast	CECT vs. Unenhanced CT
Overall	106/1464 (7.2%)	92/976 (9.4%)	168/1731 (9.7%)	0.73 (0.58–0.93)	0.75 (0.56–1.00)	0.99 (0.97–1.02)	1.02 (0.99–1.04)	−0.02 (−0.04–0.01)	0.01 (−0.02–0.03)
eGFR Subgroup									
≥ 90	52/882 (5.9%)	22/304 (7.2%)	49/771 (6.4%)	0.89 (0.61–1.28)	0.80 (0.48–1.35)	0.98 (0.95–1.01)	1.00 (0.96–1.04)	0.01 (−0.02–0.03)	0.01 (−0.03–0.05)[d]
60-89	33/407 (8.1%)	21/225 (9.3%)	31/384 (8.1%)	0.95 (0.60–1.49)	0.86 (0.48–1.52)	0.98 (0.94–1.03)	0.98 (0.91–1.06)	−0.02 (−0.08–0.03)	0.00 (−0.05–0.04)
30–59	19/155 (12.3%)	30/281 (10.7%)	62/432 (14.4%)	0.94 (0.56–1.60)	1.17 (0.63–2.15)	1.02 (0.95–1.09)	1.05 (0.97–1.12)	0.03 (−0.04–0.10)	−0.01 (−0.10–0.07)[d]
<30	2/20 (10.0%)	19/166 (11.4%)	26/144 (18.1%)	0.65 (0.15–2.92)	0.86 (0.18–4.00)	1.00 (0.89–1.12)	1.05 (0.89–1.24)	N/A[e]	N/A[e]

AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes; CI, confidence interval, CECT, contrast-enhanced computed tomography, CT, computed tomography.

[a] The average treatment of CECT measures the effect of patients undergoing CECT on the likelihood of getting AKI after matching.

[b] Odds-ratio of developing AKI comparing patients that received contrast with all patients that did not received contrast regardless if they underwent CT or not.

[c] Odds-ratio of developing AKI comparing patients that received contrast with patients that underwent CT but did receive contrast.

[d] Increased caliper of 0.2 needed to match.

[e] Perfectly colinear variables precluded the ability to perform this subgroup analysis.

for consistent measurement of altered mental status (one of the three quick Sepsis Related Organ Failure Assessment [qSOFA] criteria needed to identify patients with potential sepsis in the Emergency Department). Even where Glasgow Coma Scale (GCS) criteria were available, it was not clear from these observational data at what time the GCS score was measured making its incorporation problematic. We were also limited by the approximately 35% of patients that did not get an initial SCr value in an appropriate timeframe and 0.7% of patients who did not have sufficient vital sign or laboratory data recorded to calculate SIRS, all of whom were excluded from this analysis. Finally, while propensity score matching was used to limit selection bias associated with treatment assignment, this approach is limited by an inability to include all factors that could conceivably impact the decision to administer CM.

5. Conclusions

Sepsis is a medical emergency proven to benefit from early diagnosis and rapid initiation of treatment. As such, physicians must mobilize all available resources in the care of septic patients. For too long, outsized fear of contrast-induced AKI has led to the avoidance of CM in situations where their use was warranted. Here, we report that the risk for developing AKI following CM administration was not elevated in over four thousand patients with sepsis, including those with the lowest baseline renal function. Our findings argue against the practice of withholding CM to avoid nephropathy when administration is otherwise clinically indicated.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2019.02.003.

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