An Association Between Hyperchloremia and Acute Kidney Injury in Patients With Acute Ischemic Stroke

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Abstract

Background and Purpose: While an association between hyperchloremia and worse outcomes, such as acute kidney injury and increased mortality, has been demonstrated in hemorrhagic stroke, it is unclear whether the same relationship exists after acute ischemic stroke. This study aims to determine the relationship between moderate hyperchloremia (serum chloride ≥ 115 mmol/L) and acute kidney injury in patients with ischemic stroke. **Methods:** This is a multicenter, retrospective, propensity-matched cohort study of adults admitted for acute ischemic stroke. The primary objective was to determine the relationship between moderate hyperchloremia and acute kidney injury, as defined by the Acute Kidney Injury Network criteria. Secondary objectives included mortality and hospital length of stay. **Results:** A total of 407 patients were included in the unmatched cohort (332 nonhyperchloremia and 75 hyperchloremia) and 114 patients (57 in each group) were matched based upon propensity scores. In the matched cohort, hyperchloremia was associated with an increased risk of acute kidney injury (relative risk 1.91 [95% confidence interval 1.01-3.59]) and a longer hospital length of stay (16 vs 12 days; $P = .03$). Mortality was higher in the hyperchloremia group (19.3% vs 10.5%, $P = .19$), but this did not reach statistical significance. **Conclusions:** In this study, hyperchloremia after ischemic stroke was associated with increased rates of acute kidney injury and longer hospital length of stay. Further research is needed to determine which interventions may increase chloride levels in patients with acute ischemic stroke and the association between hyperchloremia and clinical outcomes.

Keywords

ischemic stroke, acute kidney injury, hyperchloremia, critical care, fluids and electrolytes

Background

Chloride accounts for a majority of the strong anionic charges in the blood and nearly one-third of plasma tonicity.¹ While chloride aids in regulation of fluid balance and acid-base status, a growing body of evidence among numerous populations of critically ill patients has established an association between hyperchloremia and acute kidney injury (AKI), metabolic acidosis, prolonged surgical times, and worsened morbidity and mortality.²⁻⁸ The mechanism by which hyperchloremia causes renal dysfunction has not been fully determined, but it has been shown that administration of chloride-liberal solutions induces renal vasoconstriction and results in a subsequent decline in glomerular filtration rate.^{9,10} Until recently, evidence regarding the impact of hyperchloremia on clinical outcomes in those with neurologic injuries

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was limited to those with hemorrhagic stroke. Sadan and colleagues observed an association between hyperchloremia (>111 mmol/L) and AKI in patients with subarachnoid hemorrhage (SAH).¹¹ A multicenter study of patients with intracerebral hemorrhage (ICH) identified moderate hyperchloremia (≥ 115 mmol/L) as an independent predictor of in-hospital mortality.¹² Finally, a study evaluating a mixed cohort of patients with hemorrhagic and ischemic stroke found that hyperchloremia (>110 mmol/L) development within 72 hours of admission was also associated with increased mortality.¹³ To date, no study has examined the effects of hyperchloremia solely in acute ischemic stroke (AIS), although it accounts for nearly 87% of strokes in the United States.¹⁴ Thus, we aimed to determine the relationship between moderate hyperchloremia and AKI in patients with AIS.

Materials and Methods

This multicenter, retrospective, propensity-matched cohort study included patients with AIS discharged from one of three academic medical centers (Methodist University Hospital, University of Florida Health Jacksonville, and The Ohio State University Wexner Medical Center) between August 1, 2012, and August 31, 2017. This study obtained ethics approval by institutional review boards at each of the participating centers, and the requirement for informed consent was waived at each institution. Patients were included if they presented with an AIS per International Classification of Diseases, Ninth Revision and International Classification of Diseases, 10th Revision coding, had a hospital length of stay (LOS) ≥ 7 days, and were at least 18 years of age. Patients were excluded if they were pregnant and/or lactating, had fewer than 4 chloride levels documented during the study period, had a past medical history of end-stage renal disease requiring dialysis prior to admission or serum creatinine (SCr) ≥ 2.0 mg/dL on initial presentation, were enrolled in a concurrent prospective study, underwent a craniectomy, were found to have a nonacute stroke, were hyperchloremic on admission or prior to AKI development, or were initially admitted to the hospital for a diagnosis other than AIS.

Patients were classified as either nonhyperchloremic or hyperchloremic (serum chloride ≥ 115 mmol/L) based on chloride values measured within 5 days of hospital admission. This threshold was chosen due to recent evidence in patients with ICH demonstrating that both development of hyperchloremia and incremental increases in chloride above 115 mmol/L were independently associated with mortality.^{2,12} The time frame was selected due to it being the time frame when patients with AIS are at the highest risk of developing cerebral edema that may necessitate aggressive management of fluid status and/or administration of hyperosmolar therapy.¹⁵⁻¹⁷ Serum creatinine was collected for an additional 48 hours following the 5-day period during which patients were monitored for the development of hyperchloremia or for up to 7 days after admission. This time period was selected due to evidence suggesting that

small changes in SCr observed within 48 hours after insult are linked to adverse outcomes.^{18,19} The 2 groups were analyzed to determine the rate of AKI. The use of intravenous contrast agents and nephrotoxic medications administered were assessed prior to the development of AKI. We also assessed intake of hyperosmolar therapy, maintenance fluid, or bolus fluid treatment that contained chloride, nicardipine solution admixed in sodium chloride, and mannitol. Due to variations in documentation practices at each institution, we were unable to account for chloride administration through medication diluents or salts, as well as total volume status of each patient over the entire study period.

The primary outcome was the rate of AKI, defined per the Acute Kidney Injury Network (AKIN) criteria, within the first 7 days from admission.²⁰ If a patient developed an AKI during this time frame, SCr levels were followed daily until a peak value was established, regardless of time frame, in order to properly determine the AKIN stage. Use of urine output was not used in our assessment of AKI due to lack of uniform documentation across all patients at each of the participating centers. Secondary outcomes included hospital LOS and mortality (defined as in-hospital death or discharge to hospice).

Continuous, parametric variables are described with means and standard deviation and analyzed with student *t* test. Continuous, nonparametric variables are described with mean and 25% to 75% interquartile range and analyzed with Wilcoxon rank-sum test. Categorical variables were examined with chi-square or Fisher exact test as appropriate. Potential confounding of the association between hyperchloremia and AKI was addressed using propensity score matching. Patients with hyperchloremia were matched with patients without hyperchloremia using propensity scores. Propensity scores were defined as the predicted probabilities of exposure (high chloride) conditional on observed covariates and were estimated using logistic regression.²¹ High chloride exposure was the dependent variable, and covariates noted in Supplemental Table 1 were independent variables. Patients with hyperchloremia were matched 1:1 with patients without hyperchloremia using a greedy matching algorithm without replacement. The caliper width was set to 0.2 standard deviations of the propensity score.²² In the matched sample, the association between moderate hyperchloremia and AKI was examined with a modified Poisson regression model. Poisson regression was chosen to estimate relative risks (RRs), in lieu of logistic regression, because odds ratios (ORs) are inflated compared to RR when the outcome is common, as is the case here.²³

To examine the robustness of the primary analysis, we also examined the effect of hyperchloremia on AKI using a multi-variable modified Poisson regression model. Potential confounding was evaluated using a change-in-estimate approach.²⁴ Potential confounders were added to the base model individually. Covariates that changed the RR term by $>10\%$ were retained in the final model. The final model included the following 7 adjustment variables: mechanical

Table 1. Baseline Characteristics.

Characteristic	Unmatched Cohort (n = 407)			Propensity-Matched Cohort (n = 114)		
	Nonhyperchloremia (n = 332)	Hyperchloremia (n = 75)	P	Nonhyperchloremia (n = 57)	Hyperchloremia (n = 57)	P
Age, years	64.0 (57.0-77.0)	64.0 (56.2-77.0)	.80	66.0 (58.0-78.0)	64.0 (57.0-77.0)	.73
Body mass index, kg/m ²	27.8 (24.0-33.2)	29.1 (24.5-32.7)	.71	27.1 (23.6-32.5)	29.3 (23.8-32.7)	.63
Admission NIHSS	9.0 (4.0-15.0)	16.0 (10.0-21.0)	<.001	17.0 (7.0-21.0)	15.0 (9.0-21.0)	.95
Female sex, n (%)	152 (45.8)	41 (54.7)	.20	20 (35)	28 (49)	.18
African American race, n (%)	199 (59.9)	51 (68.0)	.20	36 (63)	38 (67)	.70
Past medical history, n (%)						
Hypertension	266 (80.1)	59 (78.7)	.75	46 (81)	46 (81)	1.00
Diabetes	133 (40.1)	27 (36.0)	.60	23 (40)	22 (39)	1.00
Ischemic stroke/TIA	103 (31.0)	17 (22.7)	.16	13 (23)	14 (25)	1.00
Hyperlipidemia	102 (30.7)	17 (22.7)	.21	17 (30)	14 (25)	.67
Coronary artery disease	52 (15.7)	17 (22.7)	.17	12 (21)	11 (19)	1.00
Atrial fibrillation	42 (12.7)	8 (10.7)	.85	10 (18)	7 (12)	.60
Heart failure reduced ejection fraction	33 (9.9)	9 (12.0)	.67	7 (12)	7 (12)	1.00
Chronic kidney disease	13 (3.9)	5 (6.7)	.35	5 (9)	3 (5)	.72
Home oral anticoagulation use	26 (7.8)	4 (5.3)	.63	7 (12)	3 (5)	.32
Home antiplatelet therapy use	149 (44.9)	30 (40.0)	.52	23 (40)	24 (42)	1.00

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

^aAll data presented as median (25%-75% interquartile range) unless stated otherwise.

Figure 1. Study profile. Reasons for exclusion were not mutually exclusive. Hyperchloremic at baseline define as ≥ 115 mmol/L. Other: admitted for diagnosis other than stroke, found to have hemorrhagic etiology, age > 90 years. ESRD, end-stage renal disease; HD, hemodialysis; SCR, serum creatinine.

ventilation, heart failure, diabetes mellitus type II, antimicrobial exposure, mechanical thrombectomy, hyperlipidemia, and past history of stroke. Collinearity among candidate variables was examined with Pearson and Spearman correlation coefficients and with cross-classification of categorical variables before multivariable modeling commenced and with the variance inflation factor to assess the variables in the multivariable models.²⁵ Linearity of continuous variables was examined with fractional polynomial analysis.²⁵ All analyses were conducted using Stata/SE, version 14.2 (StataCorp, LLC, College Station, TX). Statistical

inference was based on point estimates and corresponding 95% confidence intervals (95% CIs).^{26,27}

Results

A total of 684 patients having AIS with an LOS of at least 7 days were screened for inclusion from the 3 participating centers. Reasons for exclusion are listed in Figure 1, with the most common reason being inpatient stroke. The unmatched analysis included 407 patients and the propensity-matched analysis included 114 patients.

Table 2. Treatment Variables.^a

Variable, n (%)	Unmatched Cohort (n = 407)			Propensity-Matched Cohort (n = 114)		
	Nonhyperchloremia (n = 332)	Hyperchloremia (n = 75)	P	Nonhyperchloremia (n = 57)	Hyperchloremia (n = 57)	P
IV alteplase, n (%)	79 (23.8)	26 (34.7)	.058	20 (35)	18 (32)	.84
Mechanical thrombectomy, n (%)	76 (22.9)	27 (36.0)	.027	16 (28)	17 (30)	1.00
Mechanical ventilation, n (%)	44 (13.3)	31 (41.3)	<.001	19 (33)	21 (37)	.84
Fever, n (%) ^b	36 (10.8)	27 (36.0)	<.001	17 (30)	17 (30)	1.00
Hyperglycemia, n (%) ^c	129 (38.9)	35 (46.7)	.24	23 (40)	26 (46)	.71
Hypotension, n (%) ^d	56 (16.9)	19 (25.3)	.10	16 (28)	14 (25)	.83
Vasopressor treatment, n (%)	10 (3.0)	8 (10.7)	.004	7 (12.3)	5 (8.8)	.54
Hyperosmolar therapy, n (%)	28 (8.4)	42 (56.0)	<.001	9 (15.8)	30 (52.6)	<.001
Mannitol	6 (1.8)	5 (6.7)	.04	3 (5)	3 (5)	1.00
3% Sodium chloride ^e	25 (7.5)	41 (54.7)	<.001	7 (12.3)	30 (52.6)	<.001
Nicardipine infusion, n (%)	48 (14.5)	27 (36.0)	<.001	12 (21.1)	19 (33.3)	.14
Sodium chloride based fluids, n (%) ^f	258 (77.7)	67 (89.3)	.02	50 (87.7)	49 (86.0)	.78
Milliliters received ^f	1310 (165-3324)	3915 (2109-6615)	<.001	3111 (1000-4096)	3600 (2039-6772)	.08
Milliequivalents of chloride received ^g	215.0 [30.8-541.8]	989.1 [377.2-1579.4]	<.001	479.2 (154.0-818.9)	959.4 (335.6-1593.3)	.001
Other nephrotoxic agents						
Iodinated contrast agents	269 (81.0)	56 (74.7)	.26	40 (70)	46 (81)	.28
ACE-I/ARB	145 (43.7)	41 (54.7)	.10	28 (49)	31 (54)	.71
Diuretics	95 (28.6)	21 (28.0)	1.00	18 (32)	18 (32)	1.00
NSAID	19 (5.7)	4 (5.3)	1.00	4 (7)	4 (7)	1.00
Antimicrobial agents						
Monotherapy	47 (14.2)	10 (13.3)	.85	14 (25)	6 (11)	.05
Combination therapy	35 (10.5)	27 (36.0)	<.001	18 (32)	18 (32)	1.0

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug.

^aAll data presented as median (25%-75% interquartile range) unless stated otherwise; ^b Temperature > 38.4°C.

^cBlood glucose > 180 mg/dL.

^dSystolic blood pressure < 90 mm Hg.

^eNo patients received other forms of hypertonic sodium solutions.

^fIncludes patients receiving a maintenance IV or bolus dose of 0.9% sodium chloride, 0.45% sodium chloride, dextrose 5%/0.9% sodium chloride, and dextrose 5%/0.45% sodium chloride.

^gIncludes chloride received from continuous infusion or bolus dose of 3% sodium chloride, 0.9% sodium chloride, nicardipine solution admixed in sodium chloride, dextrose 5% and 0.9% sodium chloride, dextrose 5% and 0.45% sodium chloride, and lactated ringers solution.

Unmatched Cohort

Baseline characteristics were collected, and patients were classified as nonhyperchloremic or hyperchloremic (Table 1). Patients in the unmatched cohort who developed moderate hyperchloremia were found to have significantly higher baseline National Institutes of Health Stroke Scale (NIHSS) scores (16.0 vs 9.0, $P < .001$), higher incidence of mechanical ventilation (41.3% vs 13.3%, $P < .001$), fever (36.0% vs 10.8%, $P < .001$), and mechanical thrombectomy (36.0% vs 22.9%, $P = .027$). More patients in the hyperchloremia group also received combination antimicrobial agents, vasoactive agents, and hyperosmolar therapy (Table 2). There were no statistically significant differences in baseline chloride values or SCr between the groups (Supplemental Table 2).

Patients who developed moderate hyperchloremia were more likely to develop an AKI (33.3% vs 16.9%; $P = .001$), with AKIN stage 1 injury accounting for 88% of observed events in the hyperchloremic group (Table 3) and 79% in the nonhyperchloremic group. Overall, median time to AKI from

hospital presentation among the entire cohort was 3.2 (2.1-5.1) days. Mortality was higher in the hyperchloremic group (25.3% vs 6.9%, $P < .001$), as was hospital LOS (15.5 days vs 10 days, $P < .001$; Table 3).

Propensity-Matched Cohort

After matching, baseline covariates were well balanced. Peak chloride levels were approximately 9 mmol/L higher in the hyperchloremic group (118 vs 109 mmol/L, $P < .001$). Similar to the unmatched cohort, patients with hyperchloremia in the propensity-matched analysis were more likely to develop AKI (36.8% vs 19.3%, $P = .04$; Table 3) and the development of moderate hyperchloremia continued to result in a significantly increased risk of AKI (RR 1.91 [95% CI: 1.01-3.59]; Table 4). Median time to AKI from hospital presentation among the propensity-matched cohort was 3.2 (2.3-5.2) days. Hospital LOS was longer in the hyperchloremia group (16 vs 12 days, $P = .03$). While mortality was higher in the group who

Table 3. Patient Outcomes and Discharge Status.^a

Characteristic	Unmatched Cohort (n = 407)			Matched Cohort (n = 114)		
	Nonhyperchloremia (n = 332)	Hyperchloremia (n = 75)	P	Nonhyperchloremia (n = 57)	Hyperchloremia (n = 57)	P
Mortality, n (%)	23 (6.9)	19 (25.3)	<.001	6 (10.5)	11 (19.3)	.19
Hospital LOS, days	10 (8-15)	15.5 (11-21.5)	<.001	12 (8.5-18)	16 (11-20)	.03
Treated in ICU, n (%)	124 (37.3)	52 (69.3)	<.001	35 (61.4)	34 (59.6)	.85
ICU LOS, days	3.8 (2.0-8.1)	4.5 (2.9-9.28)	.13	7.0 (3.6-11.2)	4.1 (2.5-5.9)	.35
Acute kidney injury, n (%)	56 (16.9)	25 (33.3)	.001	11 (19.3)	21 (36.8)	.04
AKIN stage 1	44 (13.3)	22 (29.3)	.001	5 (8.8)	18 (31.6)	.002
AKIN stage 2	10 (3)	3 (4)	.66	4 (7)	3 (5.3)	.70
AKIN stage 3	2 (0.6)	0 (0)	.50	2 (3.5)	0 (0)	.15
Time to AKI (days)	3.2 (2.1-5.2)	3.3 (2.2-4.8)	.80	2.7 (2.2-4.7)	3.3 (2.6-5.2)	.29

Abbreviations: AKIN, Acute Kidney Injury Network; ICU, intensive care unit; LOS, length of stay.

^aAll data presented as median (25%-75% interquartile range) unless stated otherwise.

Table 4. Outcomes in Matched Versus Unmatched Sample.

	Nonhyperchloremia, n = 332	Hyperchloremia, n = 75	Relative Risk (95% CI)	Nonhyperchloremia, n = 57	Hyperchloremia, n = 57	Relative Risk (95% CI)
No AKI	276	50	1.97 (1.32-2.95)	46	36	1.91 (1.01-3.59)
AKI	56	25		11	21	
Risk	16.9	33.3		19.3	36.8	

Abbreviations: AKI, acute kidney injury; CI, confidence interval.

developed hyperchloremia (19.3% vs 10.5%, $p = 0.19$), this difference was not statistically significant.

Secondary Analysis

The robustness of the primary analysis was validated by examining the association between hyperchloremia and AKI using a multivariable modified Poisson regression model. The multivariable adjusted results agreed with the primary analysis: RR 1.74 (95% CI: 1.11-2.71).

Discussion

Our study examined the relationship between moderate hyperchloremia and AKI in patients with AIS. In both matched and unmatched cohorts, we demonstrated that AKI occurs more commonly in patients who develop moderate hyperchloremia within the first 5 days following AIS. Patients with hyperchloremia also experienced a longer hospital stay. Similar to recent evidence in patients with other underlying neurological pathologies, hyperchloremia may have an impact on overall clinical outcomes in this patient population.¹¹⁻¹³

Our hypothesis-generating results support the need for further research into the role that hyperchloremia plays in patients with neurologic injuries. A large cohort of patients with SAH demonstrated that hyperchloremia (>111 mmol/L) was found to be strongly associated with AKI.¹¹ In patients

with ICH receiving 3% sodium chloride infusions, moderate hyperchloremia (≥ 115 mmol/L) was found to be an independent predictor of mortality (OR: 4.4 [95% CI: 1.4-13.5]).¹² Hyperchloremia (Cl ≥ 110 mmol/L) within the first 72 hours of admission was studied in critically ill patients with first-ever AIS or ICH and was associated with increased 6-month mortality and poor 6-month prognosis. Interestingly, this study excluded patients receiving hypertonic saline (3% or 10%) or other types of crystalloids except 0.9% sodium chloride during the study period.¹³ We chose to include all patients receiving treatments for cerebral edema that may contain high concentrations of sodium and chloride, as to better assess the impact of these therapies on outcomes. We also selected the threshold for hyperchloremia of chloride ≥ 115 mmol/L to provide a more accurate assessment of the true relationship between elevated chloride levels and outcomes, as we felt the chloride threshold of 110 mmol/L may result in inclusion of patients who experienced only mild, transient elevations in chloride levels. Unlike other studies, we excluded those patients who were hyperchloremic at admission. Finally, we assessed for the development of AKI over a longer period, 7 days, in order to ensure that all renal injuries following chemical insult were captured.

While the overwhelming majority of the observed AKI episodes were AKIN stage I, previous literature in those with neurologic injuries has demonstrated significantly worsened

outcomes even with mild renal injury. In a previous analysis of patients with AIS, in-hospital death was found to be 3-fold higher in patients who developed AKI, although approximately 79% of injuries reported as AKIN stage 1.²⁸ Similar evidence exists in hemorrhagic stroke. Studies including patients with spontaneous SAH have found that AKI development was associated with worsened mortality, longer LOS, and increased need for mechanical ventilation.^{29,30} Another study of patients with ICH found that AKI development, the majority of which was again AKIN stage 1, was an independent predictor of hospital mortality.¹² While not the primary focus of our study, patients with an AKI in the unmatched cohort had significantly higher mortality (19.8% vs 8.0%; $P = .002$) and there was a similar pattern of association in the propensity-matched cohort, although this did not reach statistical significance (25.0% vs 11.0%; $P = .06$).

Notably, no randomized, controlled trials have been conducted to evaluate if administration of fluids with lower chloride content improves clinical outcomes in patients with neurologic injuries. A recent cluster-randomized, multiple-crossover trial assigned 15 802 adult patients to receive either balanced crystalloids or saline (0.9% sodium chloride) and evaluated the primary outcome of major adverse kidney events within 30 days.³¹ Results demonstrated that those who received balanced crystalloids experienced lower rates of the composite outcome of death from any cause, new renal-replacement therapy, or persistent renal dysfunction when compared to saline (OR 0.91 [95% CI: 0.83-0.99]). The study included 2 notable subgroups of patients with neurologic injuries: a general population of neuro ICU patients and those with traumatic brain injuries (TBIs). Neuro ICU patients included those with brain tumors, ischemic strokes, intracranial hemorrhages, neuromuscular disorders, seizures, or other diseases of the brain and spinal cord. The overall subgroup analysis of neuro ICU patients ($n = 2817$) found similar results to the overall cohort, with use of balanced crystalloids resulting in reduced odds of the composite outcome (OR 0.77 [95% CI: 0.59-0.99]). However, the subgroup of TBI patients ($n = 1363$) found no difference (OR 1.09 [95% CI: 0.81-1.47]). Because the study included an overall mixed ICU population, the results are also indirect to those with neurologic injuries and they also do not directly assess the role of hyperchloremia on outcomes. Combined with the observational data previously discussed, we believe these subgroup analyses further support the need for future research into this area.

Our study is not without its limitations. The retrospective design limits our ability to make causal inferences or to examine long-term outcomes. We have employed extensive measures to control confounding, using both propensity-matching and multivariable regression to adjust for numerous important confounders, with each analysis showing similar results. However, as with any observational design, the possibility of residual bias cannot be completely eliminated. We also acknowledge that the exclusion of those with $\text{SCr} \geq 2.0$ at baseline may not identify all baseline renal failure. However,

we derived this definition from other studies in those with severe neurologic injuries that have recently been published in the literature.³²⁻³⁴ Our results should not be generalized to patients with CKD or those who present with an AKI. We are also unable to report data related to overall fluid status due to limitations in abstracting this retrospectively from the electronic medication record. We did report the total volume of chloride-based fluids received in those with and without hyperchloremia, as well as the total milliequivalents of chloride received. Notably, while not the focus of our study, patients with and without AKI did receive similar total volumes of chloride-based fluids in both the unmatched (2265 mL [812-5093] AKI vs 1640 mL [328-3794] non-AKI) and propensity-matched cohorts (3057 mL [1445-5960] AKI vs 3348 mL [1179-5068] non-AKI). Finally, while we assessed the receipt of numerous nephrotoxic medications, we did not document the quantity of each medication received or timing of administration prior to AKI development. Our study is unique in that this is the first study to examine the relationship between moderate hyperchloremia and AKI in a population consisting of exclusively patients with AIS.

Conclusion

We observed higher rates of AKI and longer hospital LOS in patients who developed moderate hyperchloremia following AIS. Our results are hypothesis generating and provide evidence to support future prospective trials assessing the impact of hyperchloremia in those with AIS and to determine whether certain therapies or limiting chloride exposure are associated with a higher risk of AKI.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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