Serum sodium trajectory during AKI and mortality risk

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Abstract

Introduction: Kidneys play a primary role in electrolyte homeostasis. The association between serum sodium level and mortality or the need for kidney replacement therapy during acute kidney injury has not been adequately explored.

Methods: In this prospective cohort study, we enrolled patients admitted to the Civil Hospital of Guadalajara from August 2017 to March 2020. We divided patients into five groups based on the serum sodium level trajectories up to ten days following hospitalization, 1) stable normonatremia (serum sodium 135 and 145 mEq/L), 2) fluctuating serum sodium levels (increased/decreased in and out of normonatremia), 3) uncorrected hyponatremia, 4) corrected hyponatremia, and 5) uncorrected hypernatremia. We assessed the association of serum sodium trajectories with mortality and the need for kidney replacement therapy (secondary objective).

Results: A total of 288 patients were included. The mean age was 55 ± 18 years, and 175 (60.7%) were male. Acute kidney injury stage 3 was present in 145 (51%). Kidney replacement therapy started in 72 (25%) patients, and 45 (15.6%) died. After adjusting for confounders, 10-day hospital mortality was significantly higher in group 5 (HR, 3.12; 95% CI, 1.05 to 9.24, $p = 0.03$), and kidney replacement therapy initiation was higher in group 3 (HR, 2.44; 95% CI, 1.04 to 5.70, $p = 0.03$) compared with group 1.

Conclusion: In our prospective cohort, most patients with acute kidney injury had alterations in serum sodium. Uncorrected hypernatremia was associated with death, and uncorrected hyponatremia was correlated with the need for kidney replacement therapy.

Introduction

Acute kidney injury (AKI) is a complex syndrome associated with substantial morbidity and mortality (1, 2). Serum sodium (sNa) levels during AKI is common (3, 4). Sodium is a critical electrolyte, and it affects the protein and enzyme conformations, which could impact impulse transmissions and excitation of nerve and muscle cells (5). Thus, it is not surprising to dysnatremias, defined as hyponatremia (plasma sodium < 135 mmol/L) (6), hypernatremia (plasma sodium > 145 mmol/L) (7, 8), and fluctuations in sNa (9), to be associated with complications during hospitalization, including the risk of death (10, 11). Serum Na level and its alterations during AKI and its relationship with clinical outcomes have been poorly reported (12). It has previously been observed that patients with AKI who had dysnatremia (sNa < 135 or > 145 mmol/L) at hospital admission had a higher risk of death (13). Still, it is possible that the trajectory of sNa could also be associated with unfavorable clinical outcomes. This study investigates the association between the trajectory of sNa during the hospitalization among patients with AKI and their outcomes. We hypothesize that the sNa fluctuations are related to the higher probability of death and KRT initiation.

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Methods

Study Design and Patient Population

In this prospective cohort study, we enrolled patients admitted to the Civil Hospital of Guadalajara Fray Antonio Alcalde, Mexico, from August 2017 to March 2020. This hospital is a tertiary referral academic center with 1,709 beds. All included patients were under the care of a primary medical or surgical team. We included patients

admitted in the ICU and wards with AKI and received nephrology consultation. Included patients were evaluated and followed for the first ten days of AKI diagnosis. We chose a 10-day follow-up because most AKI patients started KRT during this period (14). AKI was diagnosed by the serum creatinine (sCr) criterion of KDIGO definition (15). We only included patients who had admission serum sodium and at least three serum sodium measurements during the follow-up period available. The exclusion criteria were chronic kidney disease (CKD) stage 5 (defined as an estimated glomerular filtration rate of $< 15 \text{ ml/min/1.73 m}^2$ using the CKD-EPI Eq. (16)), chronic dialysis, hospitalization stay shorter than 48 hours, all transplant patients, pregnancy, and missing data (unable to complete the analysis). The study was approved by the Institutional Review Board and was conducted according to the Declaration of Helsinki. Informed consent was obtained from all the subjects. The protocol followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (17).

Data Collection

Clinical characteristics, demographic information, and laboratory data were collected prospectively using automated retrieval from the institutional electronic medical record system. The main predictor was the in-hospital sNa trajectory. sNa levels were measured by the direct ion-selective potentiometry technique with the AU5800 chemical analyzer (Beckman Coulter, Inc. →). For each patient, in-hospital sNa trajectory was assessed based on sNa values during the hospital stay. Missing sNa values in some cases were due to sporadic blood sample collection. We did not adjust sNa for glucose levels. Demographic and clinical variables were collected as age, diabetes, hypertension, hypothyroidism, CKD stage, smoking, cerebrovascular disease, and ischemic heart disease. The baseline serum creatinine level was defined as the most frequent value within a year before admission. The contributing risk factors of AKI, such as sepsis (Sepsis-3 criteria) (18), hypovolemia, cardiorenal syndrome (19), nephrotoxic drugs, and shock, were assessed. Prespecified biochemical data such as hemoglobin, platelets, leukocytes, glucose, urea, creatinine, potassium, chloride, phosphate, calcium, arterial pH, PCO₂, PO₂, bicarbonate, and lactate levels were also collected. Indications for KRT were diuretic-resistant fluid overload, severe hyperkalemia or metabolic acidosis, and azotemia, including encephalopathy, pericarditis, and convulsion (15, 20, 21).

Serum sodium trajectories

Figure 1 shows the groups based sNa trajectory modeling and the patterns of change for measures across multiple time points. sNa trajectories were categorized into five main patterns, 1) stable normonatremia, defined as sNa levels between 135 and 145 mEq/L, 2) fluctuating sodium, defined as sNa levels that increased/decreased in and out of normonatremia parameters, 3) uncorrected hyponatremia, defined as sNa levels $< 135 \text{ mEq/L}$, 4) corrected hyponatremia, defined as sNa levels $< 135 \text{ mEq/L}$ on hospital admission and increased to normonatremia, and finally 5) uncorrected hypernatremia, defined as sNa levels $> 145 \text{ mEq/L}$ (Fig. 1).

The primary outcome was in-hospital or 10-day follow-up mortality, whichever came first. The secondary outcome, we the need for KRT initiation.

Statistical analysis

Continuous variables are summarized as the mean $\pm$ SD unless otherwise specified. Categorical variables were summarized as numbers with percentages. Survival and KRT initiation were estimated using the Kaplan–Meier plot using the log-rank test. Patients were followed until death or ten days after hospital admission. Multivariable hazard model analysis was performed to assess the independent association between in-hospital sNa trajectories and primary and secondary outcomes, using stable normonatremia as the reference group. Model 1 was unadjusted, whereas, in model 2, we adjusted for age, sex, sex, diabetes mellitus, hypertension, smoking,

hypothyroidism, CKD, ischemic cardiopathy, sepsis, hypovolemia, cardiorenal syndrome, nephrotoxicity, AKI stage, and baseline sodium. We performed a stratified subgroup analysis by age (< 65 or ≥ 65 years), sex, diabetes mellitus, hypertension, admission surgery, sepsis, CKD, AKI stage 3, and KRT. A two-tailed P value of < 0.05 was considered statistically significant. Statistical output was generated by a software package (R Studio 1.3

Results

Baseline characteristics

Between August 2017 and March 2020, a total of 527 patients received nephrology consultation for AKI. We excluded 41 (7.7%) patients with CKD stage 5 who were on dialysis, 89 (16.8%) with a length of hospital stay < 48 hours, 71 (13.4%) with missing admission or hospital sNa levels, and 38 (7.2%) patients due to a lack of data, which led to 288 patients in the final analysis (Fig. 2). We found 81.2% of enrolled patients with dysnatremias. The clinical characteristics of patients based on in-hospital sNa trajectories are shown in Table 1. The mean age of the patients was 55 ± 18 years, and 175 (60.7%) were male. One hundred and sixteen (40.2%) had diabetes, and 16 (5.5%) had hypothyroidism. AKI stage 3 was present in 145 (50.5%) patients, and the main contributors to AKI included sepsis (50.3%) and hypovolemia (45.8%). KRT was initiated in 72 (25%) patients, and 45 (15.6%) patients died during the follow-up.

Table 1
Baseline clinical characteristics by sNa trajectories

Variables	All	Stable normonatremia	Fluctuating sodium	Uncorrected hyponatremia	Corrected hyponatremia	Uncorrected hypernatremia
Total [N (%)]	288 (100)	54 (18.5)	114 (39.5)	58 (20.1)	40 (13.8)	22 (7.6)
Age [years], mean (SD)	55.3 (18.3)	54.8 (19.0)	54.1 (18.2)	56.0 (17.7)	54.6 (19.1)	61.5 (16.5)
Gender						
Male [N (%)]	175 (60.7)	33 (61.1)	68 (59.6)	42 (72.4)	21 (52.5)	11 (50)
Female [N (%)]	113 (39.2)	21 (38.8)	46 (40.4)	16 (27.6)	19 (47.5)	11 (50)
Body Mass Index [kg/m ²], mean (SD)	26.3 (6.3)	26.3 (4.8)	26.2 (6.6)	27.1 (6.5)	26.0 (6.7)	24.7 (7.0)
Comorbidities						
Type 2 Diabetes Mellitus [N (%)]	116 (40.2)	24 (44.4)	50 (43.8)	20 (34.4)	15 (37.5)	7 (31.8)
Hypertension [N (%)]	126 (43.7)	27 (50)	54 (47.3)	20 (34.4)	15 (37.5)	10 (45.4)
Smoker [N (%)]	55 (19)	7 (12.9)	24 (21)	9 (15.5)	8 (20)	7 (31.8)
Hypothyroidism [N (%)]	16 (5.5)	4 (7.4)	7 (6.1)	2 (3.4)	3 (7.5)	0 (0)
Chronic kidney disease grade 1–4 [N (%)]	98 (34)	20 (37)	39 (34.2)	24 (41.3)	8 (20)	7 (31.8)
Cerebrovascular disease [N (%)]	12 (4.1)	1 (1.8)	7 (6.1)	1 (1.7)	1 (2.5)	2 (9)
Ischemic heart disease [N (%)]	10 (3.4)	2 (3.7)	4 (3.5)	1 (1.7)	0 (0)	3 (13.6)
AKI stages						
KDIGO-1 [N (%)]	65 (22.5)	13 (24)	30 (26.3)	15 (25.8)	3 (7.5)	4 (18.1)
KDIGO-2 [N (%)]	78 (27)	18 (33.3)	29 (25.4)	9 (15.5)	13 (32.5)	9 (40.9)
KDIGO-3 [N (%)]	145 (50.3)	23 (42.5)	55 (48.2)	34 (58.6)	24 (60)	9 (40.9)
Contributing factors to AKI						

Continuous data are presented as mean $\pm$ SD unless otherwise indicated; categoric data are presented as count (%)

Variables	All	Stable normonatremia	Fluctuating sodium	Uncorrected hyponatremia	Corrected hyponatremia	Uncorrected hypernatremia
Sepsis [N (%)]	145 (50.3)	22 (40.7)	61 (53.5)	26 (44.8)	20 (50)	16 (72.7)
Hypovolemia [N (%)]	132 (45.8)	26 (48.1)	50 (43.8)	28 (48.2)	24 (60)	4 (18.1)
Cardiorenal syndrome [N (%)]	34 (11.8)	10 (18.5)	17 (14.9)	3 (5.1)	3 (7.5)	1 (4.5)
Nephrotoxic drugs [N (%)]	52 (18)	7 (12.9)	16 (14)	18 (31)	7 (17.5)	4 (18.1)
Shock [N (%)]	92 (31.9)	13 (24)	30 (26.3)	21 (36.2)	14 (35)	14 (63.6)
Admission serum sodium [mEq/L] mean (SD)	135 (8)	136 (4)	137 (7)	128 (5)	129 (5)	146 (7)
Lowest serum sodium[mEq/L] mean (SD)	133 (7)	137 (1)	132 (5)	128 (5)	131 (5)	151 (6)
Highest serum sodium[mEq/L] mean (SD)	140 (12)	140 (2)	142 (7)	128 (17)	143 (11)	154 (6)
Hospital length of stay [days] mean (SD)	9 (2)	8.9 (2)	9.3 (1.9)	8.9 (2.6)	9.6 (1.2)	7.3 (3.5)
Kidney replacement therapy [N (%)]	72 (25)	8 (14.8)	29 (25.4)	21 (36.2)	11 (27.5)	3 (13.6)
Mortality [N (%)]	45 (15.6)	8 (14.8)	15 (13.1)	9 (15.5)	5 (12.5)	8 (36.3)
Continuous data are presented as mean $\pm$ SD unless otherwise indicated; categoric data are presented as count (%)						

The number of measured sNa was similar among the stable hyponatremia, fluctuating sNa, uncorrected hyponatremia, corrected hyponatremia, and uncorrected hypernatremia groups (3.8 $\pm$ 2.6, 5.8 $\pm$ 3.2, 3.7 $\pm$ 2.9, 5.9 $\pm$ 3.2, and 3.6 $\pm$ 2.0, respectively).

Serum sodium trajectories and hospital mortality

Among all enrollees, 45 (15.6%) died during hospitalization, including 8 (2.7%) patients with stable normonatremia, 15 (2.5%) with fluctuating sNa, 9 (3.1%) with uncorrected hyponatremia, 5 (1.7%) with corrected hyponatremia, and 8 (2.7%) with uncorrected hypernatremia. Based on the Kaplan-Meier plots, the 10-day hospital survival was 87.5% (CI 95% 0.77–0.98) for those with corrected hyponatremia, 86.8% (CI 95% 0.80–0.93) for those with fluctuating sodium, 85.2% (CI 95% 0.76–0.95) for those with stable normonatremia, 84.5% (CI 95% 0.75–0.94) in uncorrected hyponatremia, and 63.6% (CI 95% 0.46–0.87) for those with uncorrected hypernatremia, with a log-rank test $p = 0.05$

(Fig. 3). After adjusting for potential confounders, the uncorrected hypernatremia group (hazard ratio [HR], 3.12; 95% CI, 1.05 to 9.24, $p = 0.03$) compared with the stable normonatremia group was associated with significantly higher 10-day mortality (Table 2).

Table 2
The association between sNa trajectories and 10-day mortality.

Trajectory of Sodium	Mortality [Total/(events)]	Model 1 ^a		Model 2 ^b	
		HR (95% CI)	P-Value	HR (95% CI)	P-Value
Stable normonatremia	54 (8)	1 (reference)	-	1 (reference)	-
Fluctuating sodium	114 (15)	0.84 (0.35 to 1.99)	0.70	0.60 (0.24 to 1.51)	0.28
Uncorrected hyponatremia	58 (9)	1.05 (0.40 to 2.73)	0.91	0.52 (0.18 to 1.48)	0.22
Corrected hyponatremia	40 (5)	0.78 (0.25 to 2.38)	0.66	0.51 (0.15 to 1.64)	0.26
Uncorrected hypernatremia	22 (8)	2.88 (1.08 to 7.69)	0.03	3.12 (1.05 to 9.24)	0.03
HR, hazard ratio.					
^a Model 1: unadjusted					
^b Model 2: adjusted for age, sex, gender, diabetes mellitus, hypertension, smoking, hypothyroidism, chronic kidney disease, ischemic cardiopathy, sepsis, hypovolemia, cardiorenal syndrome, nephrotoxic, AKI Stage, kidney replacement therapy, and baseline sodium.					

Serum sodium trajectories and kidney replacement therapy start

During hospitalization 72 (25%) AKI patients required KRT, including 8 (2.7%) with stable normonatremia, 29 (10%) with fluctuating sodium, 21 (7.2%) with uncorrected hyponatremia, 11 (3.8%) with corrected hyponatremia, and 3 (1%) patients with uncorrected hypernatremia. Kaplan-Meier plots indicated the 10-day KRT initiation was 85.0% (CI 95% 0.76–0.95) for patients with stable normonatremia, 84.8% (CI 95% 0.70–1.00) for those with uncorrected hypernatremia, 74.2% (CI 95% 0.66–0.82) for those with fluctuating sNa, 72.5% (CI 95% 0.59–0.87) for those with corrected hyponatremia, and 62.2% (CI 95% 0.50–0.76) for those with uncorrected hyponatremia (log-rank test $p = 0.07$; Fig. 4). A significantly higher 10-day KRT initiation was noted in the uncorrected hyponatremia group when compared with the stable normonatremia group ([HR], 2.44; 95% CI, 1.04 to 5.70, $p = 0.03$) (Table 3).

Table 3
The association between sNa trajectory and the need for kidney replacement therapy.

Trajectory of Sodium	KRT [Total/(events)]	Model 1 ^a		Model 2 ^b	
		HR (95% CI)	P-Value	HR (95% CI)	P-Value
Stable normonatremia	54 (8)	1 (reference)	-	1 (reference)	-
Fluctuating sodium	114 (29)	1.78 (0.81 to 3.90)	0.14	1.64 (0.74 to 3.64)	0.22
Uncorrected hyponatremia	58 (21)	2.85 (1.26 to 6.45)	0.01	2.44 (1.04 to 5.70)	0.03
Corrected hyponatremia	40 (11)	1.95 (0.78 to 4.85)	0.14	1.42 (0.55 to 3.61)	0.46
Uncorrected hypernatremia	22 (3)	0.96 (0.25 to 3.63)	0.95	0.84 (0.21 to 3.26)	0.80
HR, hazard ratio. KRT, kidney replacement therapy.					
^a Model 1: unadjusted					
^b Model 2: adjusted for age, sex, gender, diabetes mellitus, hypertension, smoking, hypothyroidism, chronic kidney disease, ischemic cardiopathy, sepsis, hypovolemia, cardiorenal syndrome, nephrotoxic, AKI Stage, and baseline sodium.					

Subgroup analysis

We performed a subgroup analysis to confirm the increased risk of death in patients with AKI and uncorrected hypernatremia in multiple subgroups. We then repeated this process for assessment of the association between uncorrected hyponatremia and the increased KRT requirement. The subgroup analysis in unadjusted 10-day mortality in patients with uncorrected hypernatremia indicated interactions. Patients < 65 years old, males, those with diabetes mellitus, hypertension, admission by a medical service, sepsis and AKI stage 3 and KRT had worse survival (p for interaction < 0.05 for all). CKD did not have impact on mortality (p-value for interaction > 0.05) (Fig. 5). In patients with uncorrected hyponatremia, the subgroup analysis showed that patients without diabetes mellitus, those admitted to a medical service, and those with AKI stage 3 had a significantly increased risk of KRT initiation during 10-day follow-up (p-value for interaction < 0.05 for all). Meanwhile, age, sex, and hypertension did not show differences concerning KRT initiation (p for interaction > 0.05) (Fig. 6).

Discussion

In this prospective, single-center cohort, we found that > 80% of AKI patients had fluctuations in sNa during the first ten days of hospitalization. Uncorrected hypernatremia was associated with an increase (> 3-fold) in death probability, even after adjusting for potential confounders. We also found that uncorrected hyponatremia was associated with a higher need for KRT initiation, and these associations were stronger in patients with more comorbidities and worse AKI stage.

Dysnatremia and kidney injury may be separate manifestations of a common underlying disease or reflect the severity of the patient's illness and comorbidities. Many pathological conditions may lead to both dysnatremia and AKI, such as changes in the volume status. Hypo- and hypernatremia is reported to occur during AKI in all acutely ill patients (22), or patients with cardiorenal syndrome (23), cancer (24), liver transplantation (25), and in HIV-infected patients (26).

In our cohort, AKI with uncorrected hypernatremia was associated with a higher incidence of death, very similar to Darmon and colleagues' study. The authors showed that hypernatremia was associated with a greater risk of death in AKI patients by more than 4-fold (27) with short-term mortality of approximately 50–60% (7). Association of hypernatremia with force clinical outcome has been reported extensively. The etiology of hypernatremia includes free water loss (e.g., diabetes insipidus), hypotonic fluid loss (osmotic diarrhea), or hypertonic fluid gain (7). Volume depletion, which often leads to hypernatremia, is also a frequently recognized cause of AKI (28). Hypernatremia by increasing tonicity could potentially damage the cellular cytoskeleton and DNA (29). The variability in sNa levels is likely more harmful than the absolute sodium value (9). The sNa variability results in osmotic stress and induces water shifts across the cell membranes, leading to threatened cell survival (29, 30, 31). Besides, it can evoke multiple apoptotic pathways, inhibit anti-apoptotic gene expression, and induce cytokine and reactive oxygen species generation [32, 33, 34]. It also causes dysregulation of the interaction between protein phosphatase 6 and apoptosis signal-regulating kinase 3 and the cell volume recovery system (9).

The impact of sodium correction speed in hypernatremic patients on clinical outcomes is debated with scarce evidence. Historically, it has been considered that the rapid correction of hypernatremia is associated with adverse events. Olsen et al. reported that rapid correction of hypernatremia with a rate of > 0.5 mmol/L/hr could be associated with an increased risk of mortality by about 10% (35). It is noticeable that some authors suggest that the rapid correction of hypernatremia in ICU patients may not be associated with higher mortality or neurological alterations (36), even though Chauhan et al. do not describe the incidence of AKI. This evidence, along with our findings, suggests the benefits of earlier hypernatremia correction even in the presence of AKI.

We also found uncorrected hyponatremia was common among AKI patients who needed KRT. Hyponatremia leads to hypotonicity, which can cause cellular swelling and membrane rupture (29). Hyponatremia in AKI could represent a specific phenotype seen in sepsis (37), inflammation (38), or volume overload (39). Our demonstrations in the association of KRT requiring AKI in hyponatremic patients are consistent with previous studies (40).

The sNa trajectories in patients with AKI can serve as a modifiable prognostic marker used in outcome prediction and clinical complication prevention. This notion is particularly strengthened when correcting dysnatremia during hospitalization was associated with fewer complications.

Our subgroup analysis indicated that specific patient populations were more vulnerable to worse outcomes. Patients with more comorbidities had a higher risk of death, which could be due to more limited physiological reserves to allow them to counteract the negative dysnatremia consequences.

Our study has some limitations. The included cohort of patients is relatively small. Besides, we were not able to adjust sNa for the serum glucose levels. The 10-day follow-up during hospitalization was short, but it has been shown that the vast majority of patients who required KRT for AKI were initiated on KRT within the follow-up period (14). Due to the investigation's observational nature, the causal relationship between dysnatremias and clinical outcomes could not be established. Thus, our investigation solely serves as a hypothesis-generating study. Although we adjusted for known common variables associated with the studied outcomes, unmeasured confounding could not be completely ruled out. Some more rare sNa trajectories were not considered for study, although we tried to capture those that seemed most relevant to the study's objectives. Finally, we did not report the specific management strategies that were used for sodium level correction.

Our article has some strengths. To our knowledge, our cohort is the first that identifies correlations between sNa trajectories in AKI patients with death and the need for KRT initiation. The prospective observational design of our

study enhances its validity. We were able to adjust for potential confounders that reinforce the association of these variables.

In conclusion, we found that in most patients with AKI during the first ten days of hospitalization, sNa fluctuations were frequently observed. Uncorrected hypernatremia was associated with death, and uncorrected hyponatremia was correlated with the need for KRT initiation. Larger cohort studies and randomized trials are needed to confirm our findings.

Declarations

Disclosure

None.

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Figures

Figure 1

Serum sodium trajectories.

Figure 2

Flowchart of the study population

Figure 3

Kaplan-Meier for mortality based on sNa trajectory groups in the follow-up period.

Figure 4

Kaplan-Meier of the need kidney replacement therapy based on sNa trajectory groups in the follow-up period.

Subgroup	No. of patients	No. of deaths	HR	95%-CI	Interaction p
Age					
>=65 years	12	4	2.56	[0.91;7.16, p=0.07]	0.010
<65 years	10	4	3.49	[1.25;9.75, p=0.01]	
Gender					0.002
Female	11	3	2.07	[0.64;6.69, p=0.22]	
Male	11	5	3.97	[1.56;10.08, p=0.003]	
Diabetes Mellitus					<0.001
Yes	7	4	6.01	[2.14;16.85, p<0.001]	
No	15	4	1.94	[0.69;5.42, p=0.20]	
Hypertension					0.006
Yes	10	5	4.85	[1.90;12.32, p<0.001]	
No	12	3	1.77	[0.55;5.73, p=0.33]	
Admission surgical					0.001
Yes	8	2	1.88	[0.45;7.77, p=0.38]	
No	14	6	3.72	[1.57;8.81, p=0.002]	
Sepsis					0.001
Yes	16	7	4.07	[0.51;5.31, p=0.40]	
No	6	1	1.08	[1.81;9.13, p<0.001]	
CKD					0.071
Yes	7	3	3.67	[0.14;7.88, p=0.93]	
No	15	5	2.66	[1.13;11.87, p=0.02]	
AKI KDIGO 3					0.004
Yes	9	5	5.50	[1.05;6.76, p=0.03]	
No	13	3	1.64	[2.16;14.02, p<0.001]	
KRT					0.001
Yes	3	2	8.86	[0.51;5.31, p=0.40]	
No	19	6	2.47	[1.04;5.84, p=0.039]	
Overall	22	8	2.88	[1.08;7.69, p=0.03]	

0.12 0.50 1.0 2.0 4.0 38.00
Increase mortality

Figure 5

HRs of unadjusted 10-day mortality in different patient subgroups with uncorrected hypernatremia

Figure 6

HRs of unadjusted need for KRT initiation in different subgroups of patients with uncorrected hyponatremia