Associations of serum sodium levels with mortality in very elderly acute kidney injury patients

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Abstract
Background: Patients suffering from acute kidney injury (AKI) have been associated with impaired sodium. However, studies on the association of dysnatremia with all-cause mortality risk in AKI patients are particularly lacking. We examined the relationship between different levels of serum sodium and mortality among very elderly patients with AKI.

Methods: We retrospectively enrolled very elderly patients (≥ 75 years) from Chinese PLA General Hospital from 2007, to 2018. All-cause mortality was examined according to eight predefined sodium levels: <130.0 mmol/L, 130.0–134.9 mmol/L, 135.0–137.9 mmol/L, 138.0–141.9 mmol/L, 142.0–144.9 mmol/L, 145.0–147.9 mmol/L, 148.0–151.9 mmol/L, and ≥152.0 mmol/L. We estimated the risk of all-cause mortality using a multivariable adjusted Cox proportional hazard model, with a normal serum potassium level of 135.0–137.9 mmol/L as a reference.

Results: In total, 744 geriatric patients were suitable for the final evaluation. Among them, 260 (34.9%) died within 90 days; during the 1-year follow-up, 5 patients were lost to follow-up, and 383 (51.8%) died. After 90 days, the mortality rates in the eight strata were 36.1, 27.8, 19.6, 24.4, 30.7, 48.6, 52.8, and 57.7%, respectively. In the multivariable adjusted analysis, patients with sodium levels <130.0 mmol/L [hazard ratio (HR): 2.247; 95% confidence interval (CI): 1.117–4.521], from 142.0 to 144.9 mmol/L (HR: 1.964; 95% CI: 1.100–3.508), from 145.0 to 147.9 mmol/L (HR: 2.942; 95% CI: 1.693–5.114), from 148.0 to 151.9 mmol/L (HR: 3.455; 95% CI: 2.009–5.944), and ≥152.0 mmol/L (HR: 3.587; 95% CI: 2.151–5.983) had an increased risk of all-cause mortality. After 1 year, the mortality rates in the eight strata were 58.3, 47.8, 33.7, 38.9, 45.5, 64.3, 69.4, and 78.4%, respectively. In the multivariable adjusted analysis, patients with sodium levels <130.0 mmol/L (HR: 1.944; 95% CI: 1.125–3.360), from 142.0 to 144.9 mmol/L (HR: 1.681; 95% CI: 1.062–2.660), from 145.0 to 147.9 mmol/L (HR: 2.631; 95% CI: 1.683–4.112), from 148.0 to 151.9 mmol/L (HR: 2.411; 95% CI: 1.552–3.744), and ≥152.0 mmol/L (HR: 3.037; 95% CI: 2.021–4.563) had an increased risk of all-cause mortality.

Conclusion: Sodium levels outside the interval of 130.0–141.9 mmol/L were associated with increased risks of 90-day mortality and 1-year mortality in very elderly AKI patients.
Background

Acute kidney injury (AKI) is a common clinical acute critical illness that is frequently encountered in the elderly population.\textsuperscript{[1–3]} The disorder is generally characterized by an abrupt deterioration in renal function (RF) that disrupts metabolic, electrolyte and fluid homeostasis over a period of hours to days.\textsuperscript{[4–6]} Aging kidneys undergoing structural and functional changes that decrease autoregulatory capacity, systemic vasculature, and the immunological system render the elderly population highly susceptible to AKI.\textsuperscript{[7, 8]} Previous studies of AKI in the elderly population mostly examined all-cause mortality, renal prognosis, or cardiovascular events.\textsuperscript{[9, 10]} However, little work has been done on investigating electrolyte imbalances in very elderly AKI patients, such as dysnatremia and its association with mortality.\textsuperscript{[11]}

The kidneys play a central role in sodium homeostasis, and their functional decline leads to electrolyte disorders.\textsuperscript{[12]} Recently, Gao reported that compared with the reference group (136.0–144.9 mmol/L), AKI patients at the time of hospital admission with hyponatremia (< 136.0 mmol/L) or hypernatremia (≥ 145.0 mmol/L) had higher 90-day mortality rates.\textsuperscript{[12]} However, the independent or synergistic prognostic effects of abnormal serum sodium levels remain less well studied among very elderly AKI patients. In addition, the normal ranges of serum sodium levels that are applicable to such patients are still unknown.

Therefore, identifying the clinically significant normal ranges of serum sodium is an important issue for clinicians when making decisions regarding very elderly AKI patients with dysnatremia.

Materials And Methods

This was a retrospective observational study conducted at the Chinese PLA General Hospital National Clinical Research Center for Geriatric Diseases (Beijing, China). All patients aged ≥ 75 years with normal renal function who were admitted between January 2007 and December 2018 were enrolled. The study design was approved by the Clinical Ethics Committee of the Chinese PLA General Hospital. All admissions were screened and evaluated for AKI and categorized according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.
Demographic and basic data were obtained from the medical records. Serum sodium levels at the time of AKI diagnosis were recorded. Other laboratory data of interest included baseline serum creatinine (Scr) level, the Scr level at the time of AKI diagnosis, and the levels of blood urea nitrogen (BUN), uric acid, blood glucose (BG), electrolytes (K, Ca, P, and Mg), C-reactive protein (CRP), albumin, prealbumin, and hemoglobin.

The exclusion criteria were as follows: patients who had been previously diagnosed with chronic kidney disease (CKD), a hospital stay < 48 h, patients with no Scr data or only one Scr test, patients with insufficient medical records, and patients who died within 48 h of admission.

Definitions

The 2012 KDIGO-defined Scr criteria were used to identify and classify AKI.[13] The CKD Epidemiology Collaboration method was used to calculate the baseline estimated glomerular filtration rate (eGFR).[14] The baseline Scr level was the most recent measure taken in the 1–3 months before admission for AKI.[15] Sepsis was defined according to the Surviving Sepsis Campaign Bundle: 2018 update.[16] The normal sodium reference range (135.0–145.0 mmol/L) was divided into three intervals.

Furthermore, five intervals outside the normal sodium reference range were defined: one interval contained patients with a serum sodium level below 130.0 mmol/L, one contained those with a serum sodium level from 130.0 mmol/L to 134.9 mmol/L, one contained those with a serum sodium level from 135.0 mmol/L to 141.9 mmol/L, one contained those with a serum sodium level from 142.0 mmol/L to 144.9 mmol/L, one contained those with a serum sodium level from 145.0 mmol/L to 147.9 mmol/L, one contained those with a serum sodium level from 148.0 mmol/L to 151.9 mmol/L and last, one interval contained patients with a serum sodium above 152.0 mmol/L. Thus, this study contains eight sodium intervals, where the reference interval was defined as a sodium level from 135.0 to 137.9 mmol/L based on the analysis, which confirmed that the lowest mortality risk was found in this range (Table 1).

Table 1
Demographic data stratification according to serum sodium levels

| Characteristic | AKI patients | <130.0 mmol/L | 130.0–134.9 mmol/L | 135.0–137.9 mmol/L | 138.0–141.9 mmol/L | 142.0–144.9 mmol/L | 145.0–147.9 mmol/L | 148.0–151.9 mmol/L | ≥152.0 mmol/L | P-value |
|---------------|--------------|---------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|---------------|---------|
| Age (years)   | 88 (84–91)   | 30 (82–94)    | 87 (84–91)      | 87 (82–91)      | 87 (83–90)      | 87 (84–90)      | 90 (86–92)      | 89 (85–92)      | 89 (85–92)    | 0.003   |
| Male sex     | 701 (94.2)   | 108 (93.9)    | 98 (96.1)       | 150 (91.5)      | 86 (97.7)       | 67 (95.7)       | 70 (97.2)       | 70 (97.2)       | 92 (94.8)     | 0.085   |
| BMI (kg/m²)  | 23.0 ± 5.4   | 23.2 ± 5.4    | 23.1 ± 5.5      | 23.5 ± 5.5      | 23.2 ± 5.4      | 22.9 ± 5.5      | 22.6 ± 5.4      | 22.5 ± 5.4      | 22.6 ± 5.4    | 0.256   |
| (kg/m²) | 3.1 | 2.1 | 3.2 | 3.0 | 3.4 | 3.1 | 3.3 | 2.1 | 2.9 |
|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Comorbidity | | | | | | | | | |
| Coronary disease | 565 (75.9) | 24 (66.7) | 94 (81.7) | 85 (83.3) | 120 (73.2) | 60 (68.2) | 54 (77.1) | 58 (80.6) | 70 (72.2) |
| Hypertension | 546 (73.4) | 28 (77.8) | 83 (72.2) | 80 (78.4) | 121 (73.8) | 67 (76.1) | 53 (75.7) | 52 (72.2) | 62 (63.9) |
| COPD | 533 (68.7) | 20 (55.6) | 79 (68.7) | 69 (67.6) | 111 (67.7) | 59 (67.0) | 52 (74.3) | 53 (73.6) | 68 (70.1) |
| Diabetes | 283 (38.0) | 10 (27.8) | 44 (38.3) | 44 (43.1) | 64 (39.0) | 35 (39.8) | 19 (27.1) | 25 (34.7) | 42 (43.3) |
| Baseline Scr (μmol/L) | 72.0 (60.0–82.0) | 70.0 (64.0–80.0) | 72.0 (58.0–81.0) | 78.0 (62.0–86.0) | 76.0 (62.0–84.0) | 72.0 (63.0–83.0) | 69.0 (57.0–80.0) | 67.0 (56.0–80.0) | 66.0 (56.0–78.0) |
| Baseline eGFR (mL/min/1.73 m²) | 78.7 (72.2–85.4) | 78.1 (72.8–85.7) | 79.0 (73.8–84.8) | 76.8 (69.5–83.2) | 77.7 (70.2–84.8) | 78.6 (72.2–85.7) | 81.1 (72.0–85.7) | 80.4 (74.8–86.8) | 80.7 (75.7–87.1) |
| MAP (mmHg) | 78 ± 14 | 80 ± 14 | 76 ± 13 | 79 ± 15 | 81 ± 12 | 79 ± 15 | 75 ± 14 | 75 ± 15 | 76 ± 16 |
| Oliguria | 46 (6.2) | 7 (19.4) | 44 (38.3) | 22 (21.6) | 37 (22.6) | 34 (38.6) | 42 (60.0) | 50 (69.4) | 62 (63.9) |
| Others | 24 (3.2) | 9 (7.8) | 2 (2.0) | 5 (3.0) | 3 (3.4) | 0 | 1 (1.4) | 4 (4.1) | 0.044 |
| Calculators | | | | | | | | | |
| ACEI/ARBs | 414 (55.6) | 19 (52.8) | 34 (29.6) | 32 (31.4) | 59 (36.0) | 35 (39.8) | 38 (54.3) | 39 (54.2) | 56 (57.7) |
| Beta-blockers | 336 (45.2) | 17 (47.2) | 51 (44.3) | 48 (47.1) | 81 (49.4) | 41 (46.6) | 30 (42.9) | 30 (41.7) | 38 (39.2) |
| Calcium channel blockers | 306 (41.1) | 16 (44.4) | 45 (39.1) | 50 (49.0) | 69 (42.1) | 40 (45.5) | 27 (38.6) | 28 (38.9) | 31 (32.0) |
| Diuretics | 602 (80.9) | 29 (80.6) | 88 (76.5) | 85 (83.3) | 130 (79.3) | 74 (84.1) | 59 (84.3) | 61 (84.7) | 76 (78.4) |
| Lab test | | | | | | | | | |
| Scr (μmol/L) | 128.4 (115.0–145.0) | 131.5 (116.3–145.0) | 125.0 (109.0–144.0) | 128.5 (110.0–144.3) | 126.6 (115.3–142.2) | 124.7 (115.0–150.0) | 131.6 (113.8–145.1) | 136.0 (120.9–156.9) | 135.5 (116.6–149.3) |
| Peak Scr (μmol/L) | 144.0 (124.0–206.4) | 140.1 (123.3–278.5) | 136.1 (116.9–211.7) | 138.0 (122.0–180.1) | 137.0 (123.1–166.0) | 148.5 (122.8–207.6) | 171.0 (126.0–237.6) | 172.5 (131.3–267.0) | 170.0 (139.1–234.6) |
| BUN (mmol/L) | 17.5 (10.7–32.9) | 20.0 (10.0–36.6) | 14.7 (10.0–26.7) | 12.8 (9.0–20.5) | 11.4 (8.8–22.2) | 15.9 (9.6–27.3) | 23.8 (13.1–34.2) | 30.3 (21.4–41.6) | 32.5 (21.3–42.9) |
| Uric acid (mmol/L) | 366.5 (291.3–468.3) | 355.5 (255.4–421.3) | 364.0 (283.6–485.0) | 269.1 (287.9–448.2) | 356.2 (281.6–428.5) | 262.9 (267.4–468.9) | 404.0 (316.8–538.8) | 363.7 (308.3–509.3) | 336.9 (336.9–547.0) |
| BG (mmol/L) | 7.4 (5.8–10.3) | 8.3 (6.2–10.3) | 7.6 (5.8–11.2) | 7.7 (5.9–9.9) | 6.9 (5.3–8.6) | 6.4 (5.2–8.6) | 7.6 (6.1–9.4) | 7.9 (6.4–10.1) | 9.3 (7.0–12.7) |
| Hyperglycemia | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) | 1.8 (1.2–1.9) |
| < 0.001 | | | | | | | | | |
Study population

The outcome of the study was all-cause mortality within 90 days and within 1 year after AKI diagnosis.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation for parametric variables or as the median with interquartile range (with 25th and 75th percentiles) for nonparametric variables.

Categorical variables are presented as numbers (n) or percentages (%). Group comparisons were conducted using ANOVA or the Kruskal–Wallis H test for continuous variables and Pearson’s chi-square or Fisher’s exact test for categorical variables. Prognostic survival factors were identified using the Cox proportional hazards regression model. Survival probability was estimated using the Kaplan–Meier method for the eight potassium intervals, and curves were compared among groups using the log-rank test. A P-value < 0.05 was considered significant. Statistical analyses were performed using SPSS version 21.0 for Windows software (SPSS Inc., Chicago, IL, USA).

Results

Study population

In the period 2007–2018, a total of 3861 very elderly patients (aged ≥ 75 years) were hospitalized at...
the National Clinical Research Center for Geriatric Diseases, 760 of whom developed AKI during hospitalization. Of these patients, 13 were excluded because of a length of hospital stay of less than 48 hours, 3 were excluded because of missing data that was required for this study, and 744 AKI patients were suitable for the final analysis. The median age of the 744 participants was 88 years, and the majority (701, 94.2%) were male. Among all patients, 260 (34.9%) died within 90 days. During the 1-year follow-up, 5 patients were lost, and 383 (51.8%) died.

General Conditions And Clinical Characteristics According To Sodium Levels

A summary of the baseline characteristics of the study population is provided in Table 1. The overall median serum sodium level when AKI was diagnosed was 140.0 mmol/L (136.0-147.0 mmol/L). Thirty-six patients were in the low sodium group (< 130.0 mmol/L), 115 in the sodium group 130.0-134.9 mmol/L, 102 in the sodium group 135.0-137.9 mmol/L, 164 in the sodium group 138.0-141.9 mmol/L, 88 in the sodium group 142.0-144.9 mmol/L, 70 in the sodium group 145.0-147.9 mmol/L, 72 in the sodium group 148.0-151.9 mmol/L, and 72 in the sodium group ≥ 152.0 mmol/L. Age, baseline Scr, sepsis, surgery, mean aortic pressure, need for mechanical ventilation, Scr, peak Scr, BUN, peak BUN, BG, Mg, prealbumin, albumin, hemoglobin, and AKI stage differed significantly among the 8 groups at the time of AKI diagnosis. Significant interactions were also observed between serum sodium levels and both 90-day mortality (P < 0.001) and 1-year mortality (P < 0.001). The 90-day mortality rates in the eight sodium interval groups from the lowest (< 130.0 mmol/L) to the highest (≥ 152.0 mmol/L) were 36.1, 27.8, 19.6, 24.4, 30.7, 48.6, 52.8, and 57.7%, respectively. The 1-year mortality rates in the eight strata were 58.3, 47.8, 33.7, 38.9, 45.5, 64.3, 69.4, and 78.4%, respectively.

Survival analysis

Of the patients, 260 (34.9%) died during the 90-day follow-up. Survival curves for 90-day all-cause mortality across categories of serum sodium are presented in Fig. 1. As shown in Table 2, among all the deaths from AKI, 5.0% of the patients had sodium levels < 130.0 mmol/L, 12.3% had sodium levels from 130.0 to 134.9 mmol/L, 7.7% had sodium levels from 135.0 to 137.9 mmol/L, 15.4% had sodium levels from 138.0 to 141.9 mmol/L, 10.4% had sodium levels from 142.0 to 144.9 mmol/L, 13.1% had
sodium levels from 145.0 to 147.9 mmol/L, 14.6% had sodium levels from 148.0 to 151.9 mmol/L, and 21.5% had sodium levels ≥ 152.0 mmol/L.

Table 2
Association of categories of serum sodium levels with 90-day and 1-year mortality

| Characteristic | 90-day outcomes | 1-year outcomes |
|----------------|-----------------|----------------|
|                | Nonsurvivors    | Survivors      | P    | Nonsurvivors | Survivors | P |
| Sodium levels (mmol/L) | n = 260 (34.9) | n = 484 (65.1) | < 0.001 | n = 383 (51.8) | n = 356 (48.2) | < 0.001 |
| < 130.0        | 13 (5.0)        | 23 (4.8)       | 21 (5.5) | 15 (4.2) |
| 130.0–134.9    | 32 (12.3)       | 83 (17.1)      | 54 (14.1) | 59 (16.6) |
| 135.0–137.9    | 20 (7.7)        | 82 (16.9)      | 34 (8.9) | 67 (18.8) |
| 138.0–141.9    | 20 (7.7)        | 82 (16.9)      | 34 (8.9) | 67 (18.8) |
| 142.0–144.9    | 40 (15.4)       | 124 (25.6)     | 63 (16.4) | 99 (27.8) |
| 145.0–147.9    | 36 (7.4)        | 82 (16.9)      | 45 (11.7) | 25 (7.0) |
| 148.0–151.9    | 34 (7.0)        | 82 (16.9)      | 50 (13.1) | 22 (6.2) |
| ≥ 152.0        | 56 (21.5)       | 41 (8.5)       | 76 (19.8) | 21 (5.9) |

Table 3
Multivariate Cox proportional hazard model analysis of risk factors for mortality

| Risk factor | 90-day mortality | 1-year mortality |
|-------------|------------------|------------------|
|             | HR, 95% CI       | P                | HR, 95% CI      | P                |
| MAP         | 0.960, 0.951–0.968 | < 0.001         | 0.979, 0.972–0.986 | < 0.001         |
| Albumin     | -                 | -                | 0.906, 0.887–0.924 | < 0.001         |
| Sodium levels (mmol/L) | Reference | 1.117–4.521, 0.023 | 1.944, 1.125–3.360, 0.017 |
|             | 135.0–137.9 | Reference | - | Reference | Reference - |
|             | < 130.0        | 2.247, 1.117–4.521, 0.023 | 1.944, 1.125–3.360, 0.017 |
|             | 130.0–134.9    | 0.825, 0.825–2.522, 0.199 | 1.436, 0.935–2.207, 0.099 |
|             | 138.0–141.9    | 0.840, 0.840–2.463, 0.186 | 1.428, 0.938–2.173, 0.097 |
|             | 142.0–144.9    | 1.100, 1.100–3.508, 0.022 | 1.681, 1.062–2.660, 0.027 |
|             | 145.0–147.9    | 1.693, 1.693–5.114, < 0.001 | 2.631, 1.683–4.112, < 0.001 |
|             | 148.0–151.9    | 2.009, 2.009–5.944, < 0.001 | 2.411, 1.552–3.744, < 0.001 |
|             | ≥ 152.0        | 3.587, 3.587–2.151, < 0.001 | 3.037, 2.021–4.563, < 0.001 |

During the 1-year follow-up, 5 patients were lost, and 383 (51.8%) died. Survival curves for 1-year all-cause mortality across categories of serum sodium are presented in Fig. 2. Among all the deaths from AKI, 5.5% of the patients had sodium levels < 130.0 mmol/L, 14.1% had sodium levels from 130.0 to 134.9 mmol/L, 8.9% had sodium levels from 135.0 to 137.9 mmol/L, 16.4% had sodium levels from 138.0 to 141.9 mmol/L, 10.4% had sodium levels from 142.0 to 144.9 mmol/L, 11.7% had sodium levels from 145.0 to 147.9 mmol/L, 13.1% had sodium levels from 148.0 to 151.9 mmol/L, and 19.8% had sodium levels ≥ 152.0 mmol/L.

In the multivariable adjusted analysis, patients with sodium levels < 130.0 mmol/L [hazard ratio (HR): 2.247; 95% confidence interval (CI): 1.117–4.521; P = 0.023], from 142.0 to 144.9 mmol/L (HR: 1.964;
95% CI: 1.100–3.508; P = 0.022), from 145.0 to 147.9 mmol/L (HR: 2.942; 95% CI: 1.693–5.114; P < 0.001), from 148.0 to 151.9 mmol/L (HR: 3.455; 95% CI: 2.009–5.944; P < 0.001), and ≥ 152.0 mmol/L (HR: 3.587; 95% CI: 2.151–5.983; P < 0.001) had relatively higher 90-day mortality rates. Significant interactions were also observed between serum sodium levels and 1-year mortality: patients with sodium levels < 130.0 mmol/L (HR: 1.944; 95% CI: 1.125–3.360; P = 0.017), from 142.0 to 144.9 mmol/L (HR: 1.681; 95% CI: 1.062–2.660; P = 0.027), from 145.0 to 147.9 mmol/L (HR: 2.631; 95% CI: 1.683–4.112; P < 0.001), from 148.0 to 151.9 mmol/L (HR: 2.411; 95% CI: 1.552–3.744; P < 0.001), and ≥ 152.0 mmol/L (HR: 3.037; 95% CI: 2.021–4.563; P < 0.001) had relatively higher 1-year mortality rates.

Discussion

Sodium is the main electrolyte responsible for serum osmolarity.\[17\] Patients suffering from AKI have impaired sodium homeostasis. Dysnatremia is the most common electrolyte abnormality in clinical practice, as our study found (52.4%).\[11\] No studies have independently or simultaneously investigated the prognostic role of such electrolytes among very elderly patients with AKI. This study analyzed the 90-day mortality and 1-year mortality risks in relation to different serum sodium intervals in very elderly AKI patients. It was not surprising that sodium levels outside the normal range (Na < 130.0 and > 145.0 mmol/L) were associated with an increased mortality risk; it was unexpected that one normal sodium level (Na: 142.0–144.9 mmol/L) was also associated with a significantly increased mortality risk in AKI patients. In the elderly population, the incidence of electrolyte imbalance is expected to be higher because of organ decline, decreased physiologic reserves, frailty, and the higher prevalence of disability and functional impairment.\[18–20\] Kidneys are responsible for maintaining water homeostasis, and AKI could magnify the effect of dysnatremia on the clinical consequences. Normal ranges of serum sodium levels within 135.0–145.0 mmol/L used in clinical settings are determined mainly based on healthy subjects, and whether these values are applicable to elderly patients with complex comorbidities is still unknown.\[21\] Through interfering with tubular functions, AKI disturbs the
physiological regulation of electrolyte homeostasis, which could be more prominent in the elderly population. Previous studies have consistently reported that electrolyte imbalances, including dysnatremia and dyskalemia, are associated with worse in-hospital outcomes. Furthermore, the adverse impact of dysnatremia on clinical outcomes might be independent of the presence of initial AKI.

Hypernatremia is characterized by a deficit of total body water relative to the total body sodium level and is defined as a serum sodium concentration exceeding 145 mmol/L.\cite{22} Hypernatremia in the geriatric population is a common disorder associated with significant mortality. Older people are predisposed to developing hypernatremia because of age-related physiologic changes such as decreased thirst drive, impaired urinary concentrating ability, and reduced total body water.\cite{23} Medications may also exacerbate this predisposition. Clinical data reported that hypernatremia is present in approximately 2.0% of patients older than 65 years but in almost 4.8% of those older than 75 years admitted to the hospital.\cite{24} In a retrospective study involving 8,441 older patients admitted to the ICU, approximately 3.6% had hypernatremia on admission, and 15.3% developed hypernatremia during hospitalization;\cite{25} the mortality rate in those admitted with hypernatremia was approximately 33.3%, while patients without hypernatremia had a mortality rate of 18.1%.\cite{25} If patients had normal serum sodium levels on admission and developed mild hypernatremia (145.0–150.0 mmol/L) or moderate to severe hypernatremia (> 150.0 mmol/L) in the ICU, the mortality rates increased to 29.5% and 46.2%, respectively.\cite{25} Other studies have confirmed these findings: mortality increases with increasing serum sodium level, and even mild hypernatremia is associated with significant mortality in hospitalized elderly patients, even after accounting for confounders.\cite{25-27}

Hyponatremia, defined as a serum sodium concentration below 135 mmol/L, is the most common electrolyte problem seen in hospitalized patients.\cite{22} Advanced age is an independent risk factor for the development of hyponatremia due to the decreased ability of the body to handle stresses related
to salt and water balance. Moreover, drugs such as thiazides and nonsteroidal anti-inflammatory agents commonly used in this age group contribute to a decreased renal ability to excrete free water. Critically ill patients also demonstrate impaired renal capacity to excrete free water. Hyponatremia has been observed in 14.5–37.9% of patients upon hospital admission,[28-30] while rates of hospital-acquired hyponatremia range from 11.0 to 38.2%. [29, 31, 32] Mortality rates vary significantly based on the population studied, and in several studies, hyponatremia has been associated with an increased risk of death.[28-32]

The treatment and prevention of AKI remains a major challenge for intensive care physicians and nephrologists. When managing severe AKI, whether to provide renal replacement therapy (RRT) and, if it is needed, when to initiate it are unclear. It is widely accepted that if there are life-threatening complications of AKI, such as hyperkalemia or metabolic acidosis, RRT should be initiated immediately. However, in the absence of such complications, the appropriate timing of the initiation of RRT remains unclear. A significant interaction between serum sodium levels and mortality was observed in our study (P interaction: <0.001 for 90-day mortality and < 0.001 for 1-year mortality). Across different sodium strata, higher and lower serum sodium levels were both associated with an increased risk of mortality among patients with AKI. Hypernatremia has been poorly assessed in AKI, probably because according to a previous report, more AKI patients suffer from hyponatremia (Na⁺ < 135 mmol/L) than hypernatremia (Na⁺ > 145 mmol/L) (27.0% vs 5.7%) when admitted to the ICU.[33] However, the percentage of patients with hypernatremia was 32.1% compared with 20.3% of the patients with hyponatremia in our study. Both hyponatremia and hypernatremia can have direct adverse effects on the function of various organs, including the brain, heart, and musculoskeletal system, and subsequently increase mortality. Dysnatremia may be a potential target for correction for clinicians. However, whether correcting dysnatremia could improve outcomes should be evaluated in future studies.

Strengths And Limitations

There were also several limitations of this study. First, this was a single-center retrospective analysis,
and we could only establish an association rather than a causal relationship. In addition, different results could be reached when using patient records from other centers. Therefore, subject selection bias cannot be ignored. Second, we only analyzed sodium levels at the time of AKI diagnosis, and these levels could change over time (e.g., initiating electrolyte therapy). Third, although we attempted to account for a number of potential confounders in the multivariable analyses, it is plausible that other unidentified variables may have influenced the results. Finally, we used all-cause mortality rather than cause-specific mortality, which was also a major limitation.

**Conclusion**

Sodium levels outside the interval of 130.0-141.9 mmol/L were associated with increased 90-day mortality and 1-year mortality risks in very elderly AKI patients.

**Abbreviations**

AKI = acute kidney injury; BMI = body mass index; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; MAP = mean aortic pressure; 1 mmHg, 0.133 kPa. MV = mechanical ventilation; Scr = serum creatinine; BUN = blood urea nitrogen; BG = blood glucose; RRT = renal replacement therapy

**Declarations**

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**Availability of data and material**

All data generated and/or analyzed during this study are included in this published article.

**Authors’ contributions**

QL participated in the conception and design of the study, did the statistical analyses, reviewed the literature, analyzed and interpreted the data, and drafted the manuscript. LP and ZM participated in the conception and design of the study, acquisition of data, analyzed and interpreted the data. HK
was involved in design and in acquisition of data and helped to revise the manuscript critically for important content. FZ conceived of the study, participated in its design, and helped to revise manuscript. All authors read and approved the final manuscript.

**Ethical approval**

The study design was approved by the Clinical Ethics Committee of the Chinese PLA General Hospital.

**Informed consent**

For this type of study, formal consent is not required.

**Consent for publication**

The manuscript has been read and its submission approved by all coauthors.

**Competing interests**

The authors declare that they have no competing interests.

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Figures

**Figure 1**

Kaplan-Meier plot of cumulative rates of 90-day mortality stratified by serum sodium levels (log-rank test: P < 0.001)
Figure 1

Kaplan–Meier plot of cumulative rates of 90-day mortality stratified by serum sodium levels

(log-rank test: $P < 0.001$)
Figure 2

Kaplan-Meier plot of cumulative rates of 1-year mortality stratified by serum sodium levels

(log-rank test: $P < 0.001$)
Figure 2

Kaplan–Meier plot of cumulative rates of 1-year mortality stratified by serum sodium levels

(log-rank test: $P < 0.001$)