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Original Article

Association of serum potassium level with early and late mortality in very elderly patients with acute kidney injury

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ABSTRACT

Background: The kidneys play a central role in serum potassium (K^+) homeostasis, and their dysfunction leads to electrolyte disorders. We aimed to examine the relationship between different levels of K^+ and mortality among very elderly patients with acute kidney injury (AKI).

Methods: We retrospectively enrolled very elderly patients (≥75 years) with AKI from the hospital information system of the Chinese PLA General Hospital from January 1, 2007 to December 31, 2018. All-cause mortality was examined according to six predefined K^+ levels: <3.50 mmol/L, 3.50–3.79 mmol/L, 3.80–4.09 mmol/L, 4.10–4.79 mmol/L, 4.80–5.49 mmol/L, and ≥5.50 mmol/L. We estimated the risk of all-cause mortality using the multivariable adjusted Cox proportional hazard model with the normal K^+ level at 3.50–3.79 mmol/L as a reference.

Results: In total, 747 patients were deemed suitable for the final evaluation. The median age of the 747 participants was 88 (84–91) years. After 90 days, the mortality rates in the six strata were 28.3%, 21.9%, 30.1%, 35.4%, 45.2%, and 58.3%, respectively. In the multivariable adjusted analysis, patients with K^+ levels of 4.10–4.79 mmol/L (hazard ratio [HR]: 1.638; 95% confidence interval [CI]: 1.016–2.642), 4.80–5.49 mmol/L (HR: 2.585; 95% CI: 1.524–4.384), and ≥5.50 mmol/L (HR: 2.587; 95% CI: 1.495–4.479) had an increased risk of all-cause mortality. After 1 year, the mortality rates in the six strata were 44.8%, 41.1%, 45.1%, 51.8%, 63.1%, and 76.3%, respectively. In the multivariable adjusted analysis, patients with K^+ levels of 4.10–4.79 mmol/L (HR: 1.452; 95% CI: 1.014–2.079), 4.80–5.49 mmol/L (HR: 2.151; 95% CI: 1.427–3.241), and ≥5.50 mmol/L (HR: 2.341; 95% CI: 1.514–3.620) had an increased risk of all-cause mortality.

Conclusion: Increased serum K^+ levels, including levels of 4.10–5.49 mmol/L and ≥5.50 mmol/L, were associated with a significantly increased short- and long-term risk of death. Serum K^+ has the potential to be a marker of disease severity among very elderly patients with AKI.

Introduction

Potassium (K^+) is a ubiquitous cation contained mostly within the intracellular fluid. Serum K^+ levels are maintained between 3.5 mmol/L and 5.5 mmol/L by renal excretion and the shift between intracellular and extracellular fluid compartments.[1] The kidneys play a central role in K^+ homeostasis, and their functional decline leads to electrolyte imbalance and associated disorders.[2] Hyperkalemia is one of the major electrolyte disturbances in patients with acute kidney injury (AKI). Severe hyperkalemia (serum K^+ of at least 6.5 mmol/L) is a potentially life-threatening electrolyte disorder that may require renal replacement therapy (RRT).[3] Hence, management of such electrolyte imbalance is crucial according to clinical guidelines and is widely practiced.

AKI is a common, acute, and critical illness with various etiologies in the elderly and is encountered in multiple clinical specialties. In elderly patients, there are numerous factors including structural and functional changes of the aging kidney, underlying comorbidities, and medication use (e.g., angiotensin-

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converting enzyme inhibitors [ACEIs], angiotensin II receptor blockers [ARBs], or diuretics) that might affect the serum K^+levels.[4,5] Therefore, identifying the clinical significance of serum K^+ beyond the normal range is an important issue for clinicians.

Recently, levels both below and above the clinically accepted normal range of serum K^+ at admission were found to be associated with excess mortality in a U-shaped relationship among hospitalized patients with diseases such as hypertension, heart failure, or myocardial infarction.[6–8] Correspondingly, Gao et al.[2] reported that compared with the reference group (3.7–4.7 mmol/L), hypokalemia (<3.7 mmol/L) or hyperkalemia (≥4.8 mmol/L) in AKI patients at hospital admission was associated with an excessive 90-day mortality. However, the independent or synergistic prognostic effects of abnormal serum K^+ levels remain less studied among elderly patients with AKI. In addition, the acceptable ranges of serum K^+ levels applicable to such patients remain unknown.

In this study, we aimed to examine the possible relationships between serum K^+ levels and all-cause mortality, and demonstrated that elevation of serum K^+ levels was an independent risk factor for worse prognosis regardless of AKI severity or impaired renal function in very elderly patients after AKI onset.

Methods

Study design, setting, and population

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 to the general ward from January 2007 to December 2018 were enrolled. The study design was approved by the Clinical Ethics Committee of the Chinese PLA General Hospital (Number: S2017–054–01). Given the observational retrospective nature of the study, the need for written informed consent from each patient was waived. Patient data were anonymized and non-identifiable. This study was conducted in accordance with the tenets of the Declaration of Helsinki. 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 noted from the medical records and were compared among groups of patients stratified according to the following K^+ levels: <3.50 mmol/L, 3.50–3.79 mmol/L, 3.80–4.09 mmol/L, 4.10–4.79 mmol/L, 4.80–5.49 mmol/L, and >5.50 mmol/L. The serum K^+ interval of 3.50–3.79 mmol/L was used as a reference for statistical analysis, which confirmed that the lowest mortality risk was found in this range. Hypokalemia was defined as serum K^+<3.50 mmol/L and hyperkalemia as serum K^+≥5.50 mmol/L.[9]

Clinical data including the demographic profile (age, sex, and body mass index [BMI]); comorbidities (such as history of hypertension, coronary artery disease, chronic obstructive pulmonary disease [COPD], and diabetes mellitus); etiology of AKI (induced by sepsis, hypovolemia, cardiovascular events, nephrotoxic drugs, surgery, or others); pharmacotherapy including ACEI/ARB, beta-blockers, calcium-channel blockers, potassium-sparing diuretics, and potassium supplement; need for RRT; need for mechanical ventilation (MV); urine output; and mean arterial pressure (MAP) were noted for all patients. Other laboratory data of interest included baseline serum creatinine (Scr) and Scr at AKI diagnosis, as well as blood urea nitrogen (BUN), uric acid, blood glucose (BG), electrolytes (sodium [Na], calcium [Ca], phosphate [P], and magnesium [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), hospital stay <48 h, patients with no Scr or only one Scr result, patients with insufficient medical records, and those who died within 48 h of admission.

Definitions

The 2012 KDIGO-defined Scr criteria were used to identify and classify AKI, e.g., a Scr increase ≥0.3 mg/dL (≥26.5 μmol/L) within 48 h, or an increase to ≥1.5-fold above the baseline within the last 7 days.[10] The CKD Epidemiology Collaboration was used to calculate the baseline estimated glomerular filtration rate (eGFR).[11] The baseline Scr level was the most recent measure taken in the 1–3 months before admission for AKI.[12] Sepsis was defined according to the Surviving Sepsis Campaign Bundle: 2018 update.[13]

The normal K^+ reference range (3.50–5.50 mmol/L) was divided into four intervals. Furthermore, two intervals outside the normal K^+ reference range were defined: one interval containing patients with a serum K^+ value <3.50 mmol/L and one interval containing patients with a serum K^+ value >5.50 mmol/L. Thus, this study contained six K^+ intervals, where the reference interval was defined as serum K^+ from 3.50 mmol/L to 3.79 mmol/L based on an analysis that confirmed that the lowest mortality risk was found in this range [Table 1].

Outcomes

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

Statistical analysis

Continuous variables of parametric data are presented as the mean ± standard deviation (SD) or as 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 analysis of variance (ANOVA) or the Kruskal–Wallis H-test for continuous variables and Pearson's chi-squared 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 six potassium intervals, and curves were compared among groups using the log-rank test. A P-value of < 0.05 was considered to indicate statistical significance. Statistical analyses were performed using SPSS version 21.0 for Windows software (IBM Corporation, Armonk, NY, USA).

Table 1
Demographic stratification according to serum potassium (*K*+) levels.

Characteristic	<3.50 mmol/L (*n*=60, 8.0%)	3.50–3.79 mmol/L (*n*=96, 12.9%)	3.80–4.09 mmol/L (*n*=153, 20.5%)	4.10–4.79 mmol/L (*n*=274, 36.7%)	4.80–5.49 mmol/L (*n*=104, 13.9%)	≥5.50 mmol/L (*n*=60, 8.0%)	t/χ^2	*P*-value
Age (years)	88 (83–91)	87 (83–91)	88 (84–91)	87 (84–91)	88 (84–92)	87 (85–91)	1.215	0.943
Male sex	54 (90.0)	92 (95.8)	143 (93.5)	260 (94.9)	98 (94.2)	57 (95.0)	2.594	0.762
BMI (kg/m^2)	22.1 ± 3.3	23.4 ± 3.3	23.1 ± 2.9	22.9 ± 3.1	23.1 ± 3.2	23.0 ± 2.8	1.408	0.219
Comorbidity								
Coronary disease	45 (75.0)	77 (80.2)	112 (73.2)	205 (74.8)	79 (76.0)	50 (83.3)	3.604	0.608
Hypertension	41 (68.3)	71 (74.0)	116 (75.8)	196 (71.5)	86 (82.7)	39 (65.0)	8.535	0.129
COPD	39 (65.0)	68 (70.8)	100 (65.4)	190 (69.3)	69 (66.3)	45 (75.0)	2.764	0.736
Diabetes	17 (28.3)	40 (41.7)	59 (38.6)	102 (37.2)	39 (37.5)	28 (46.7)	4.927	0.425
Baseline Scr (μmol/L)	75.0 (62.0–86.0)	77.0 (64.0–85.0)	73.0 (60.0–83.0)	72.0 (62.0–83.0)	70.0 (56.0–78.0)	64.0 (50.0–73.0)	23.775	<0.001
Baseline eGFR ($mL \cdot min^{-1} \cdot 1.73\ m^2$)	76.9 (71.9–82.5)	78.2 (70.2–83.6)	78.3 (70.7–85.5)	78.4 (71.7–84.8)	80.3 (75.3–86.9)	83.7 (78.0–91.1)	19.585	0.001
Etiology of AKI								
Sepsis	26 (43.3)	44 (45.8)	50 (32.7)	117 (42.7)	44 (42.3)	31 (51.7)	8.436	0.134
Hypovolemia	12 (20.0)	18 (18.8)	39 (25.5)	54 (19.7)	23 (22.1)	15 (25.0)	2.927	0.711
Cardiovascular events	10 (16.7)	13 (13.5)	23 (15.0)	44 (16.1)	17 (16.3)	5 (8.3)	2.772	0.735
Nephrotoxicity	6 (10.0)	17 (17.7)	22 (14.4)	28 (10.2)	9 (8.7)	7 (11.7)	5.973	0.309
Surgery	1 (1.7)	3 (3.1)	15 (9.8)	21 (7.7)	8 (7.7)	1 (1.7)	11.859	0.037
Others	5 (8.3)	1 (1.0)	4 (2.6)	10 (3.6)	3 (2.9)	1 (1.7)	6.458	0.264
Clinical conditions								
MAP (mmHg)	79 ± 16	81 ± 14	79 ± 15	77 ± 14	77 ± 13	73 ± 14	3.197	0.007
Oliguria	1 (1.7)	5 (5.2)	6 (3.9)	12 (4.4)	13 (12.5)	9 (15.0)	17.831	0.003
MV	18 (30.0)	30 (31.3)	54 (35.3)	111 (40.5)	52 (50.0)	36 (60.0)	21.259	0.001
Pharmacotherapy								
ACEI/ARB	32 (53.3)	56 (58.3)	96 (62.7)	149 (54.4)	56 (53.8)	26 (43.3)	7.529	0.184
Beta-blockers	22 (36.7)	53 (55.2)	68 (44.4)	118 (43.1)	54 (51.9)	21 (35.0)	10.598	0.060
Calcium channel blockers	25 (41.7)	35 (36.5)	69 (45.1)	114 (41.6)	44 (42.3)	19 (31.7)	4.168	0.525
Potassium-sparing diuretics	45 (75.0)	75 (78.1)	124 (81.0)	216 (78.8)	93 (89.4)	52 (86.7)	8.799	0.117
Potassium supplement	30 (50.0)	58 (60.4)	93 (60.8)	163 (59.5)	70 (67.3)	35 (58.3)	4.960	0.421
Laboratory parameters								
Scr (μmol/L)	124.5 (107.8–142.6)	126.0. (113.7–138.5)	124.0 (112.3–139.4)	129.2 (116.4–143.7)	135.2 (118.9–154.8)	139.0 (120.7–161.0)	22.772	0.001
Peak Scr (μmol/L)	143.4 (126.5–178.0)	135.5 (116.8–179.8)	137.0 (119.3–170.2)	146.5 (126.5–221.0)	157.4 (130.1–285.8)	171.0 (137.1–247.9)	28.084	<0.001
BUN (mmol/L)	11.0 (7.7–16.9)	10.0 (7.4–16.7)	11.2 (8.1–17.8)	12.6 (9.0–19.8)	16.2 (11.2–26.8)	21.5 (13.9–35.4)	76.687	<0.001
Peak BUN (mmol/L)	16.3 (11.4–27.3)	13.8 (8.5–25.9)	14.2 (9.1–25.6)	16.8 (10.5–32.7)	26.3 (13.2–42.6)	30.3 (20.0–47.9)	65.888	<0.001
Uric acid (mmol/L)	364.0 (257.0–443.8)	356.6 (281.0–450.3)	348.4 (274.1–454.1)	362.8 (281.0–441.6)	406.1 (328.5–506.5)	416.6 (332.5–532.5)	23.178	<0.001
BG (mmol/L)	7.5 (5.7–10.6)	7.6 (5.8–9.3)	7.0 (5.7–10.0)	7.6 (5.8–10.2)	7.7 (6.0–11.1)	7.4 (5.9–10.4)	3.937	0.559
K (mmol/L)	3.3 (3.1–3.4)	3.6 (3.5–3.7)	3.9 (3.8–4.0)	4.3 (4.2–4.5)	5.0 (4.9–5.2)	5.8 (5.6–6.1)	699.150	<0.001
Na (mmol/L)	142.0 (136.0–149.0)	143.0 (138.0–149.0)	140.0 (137.0–146.0)	140.0 (135.0–146.0)	139.0 (134.0–146.0)	141.0 (136.0–149.0)	12.430	0.029
Ca (mmol/L)	2.2 (2.0–2.3)	2.2 (2.0–2.3)	2.2 (2.1–2.3)	2.2 (2.1–2.3)	2.2 (2.1–2.5)	2.3 (2.1–2.5)	12.889	0.024
P (mmol/L)	1.0 (0.8–1.2)	1.1 (0.9–1.4)	1.2 (0.9–1.4)	1.2 (1.0–1.4)	1.3 (1.1–1.6)	1.5 (1.1–1.7)	52.543	<0.001
Mg (mmol/L)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.8–1.1)	11.475	0.043
CRP (mmol/L)	5.0 (2.4–10.6)	3.5 (1.7–8.2)	3.7 (2.1–8.9)	4.0 (1.7–10.0)	5.3 (2.0–9.4)	5.0 (2.2–8.6)	3.523	0.620
Albumin (g/L)	34.1 ± 6.3	34.8 ± 4.4	34.5 ± 5.0	34.0 ± 5.6	34.7 ± 6.5	32.9 ± 6.1	1.193	0.311
Prealbumin (g/L)	165.0 (134.0–239.0)	191 (141–227)	173 (144–225)	178 (134–227)	179 (127–247)	162 (130–208)	3.880	0.567
Hemoglobin (g/L)	116 ± 22	115 ± 20	114 ± 22	112 ± 22	108 ± 24	104 ± 24	3.043	0.010
AKI stage							43.466	<0.001
1	28 (46.7)	56 (58.3)	77 (50.3)	118 (43.1)	33 (31.7)	13 (21.7)		
2	22 (36.7)	16 (16.7)	42 (27.5)	67 (24.5)	25 (24.0)	19 (31.7)		
3	10 (16.7)	24 (25.0)	34 (22.2)	89 (32.5)	46 (44.2)	28 (46.7)		
Outcomes								
RRT	0	0	0	3 (1.1)	1 (1.0)	0	5.483	0.360
90-day mortality	17 (28.3)	21 (21.9)	46 (30.1)	97 (35.4)	47 (45.2)	35 (58.3)	29.113	<0.001
1-year mortality	26 (44.8)*	39 (41.1)†	69 (45.1)	142 (51.8)	65 (63.1)†	45 (76.3)†	27.696	<0.001

Data are shown as *n* (%), mean ± SD or median (interquartile range).
*2 patients lost during 1-year follow-up. †1 patient lost during 1-year follow-up. ACEI: Angiotensin–converting enzyme inhibitors; AKI: Acute kidney injury; ARBs: Angiotensin receptor blockers; BG: Blood glucose; BMI: Body mass index; BUN: Blood urea nitrogen; COPD: Chronic obstructive pulmonary disease; CRP: C–reactive protein; eGFR: Estimated glomerular filtration rate; MAP: Mean arterial pressure; MV: Mechanical ventilation; RRT: Renal replacement therapy; Scr: Serum creatinine; SD: Standard deviation.

Results

Study population

In the period from January 2007 to December 2018, a total of 3861 very elderly patients (age, ≥75 years) were hospitalized at the National Clinical Research Center for Geriatric Diseases; 760 of these patients developed AKI during hospitalization, and 747 AKI patients were deemed suitable for the final analysis in this study. The median age of the 747 patients was 88 years, and the majority (704, 94.2%) were male. Among all patients, 263 (35.2%) died within 90 days. During the 1-year follow-up, 5 patients were lost to follow-up, and 386 (52.0%) died.

General conditions and clinical characteristics according to K^+ *levels*

A summary of the baseline characteristics of the study population is provided in Table 1. Sixty patients were in the low K^+ group (<3.50 mmol/L), 96 in the 3.50–3.79 mmol/L K^+ group, 153 in the 3.80–4.09 mmol/L K^+ group, 274 in the 4.10–4.79 mmol/L K^+ group, 104 in the 4.80–5.49 mmol/L K^+ group, and 60 in the ≥5.50 mmol/L K^+ group. With the increase in serum K^+ levels, the patients' baseline Scr value decreased (χ^2=23.775, P<0.001), but their baseline eGFR increased (χ^2=19.585, P=0.001). Accordingly, the prevalence of oliguria (χ^2=17.831, P=0.003) and need for MV (χ^2=21.259, P=0.001) became significantly higher than the K^+ level at 3.50–3.79 mmol/L with the increase in serum K^+levels. MAP and hemoglobin levels decreased, while Scr, peak Scr, BUN, peak BUN, uric acid, Na, Ca, P, and Mg levels increased at the time of AKI diagnosis. Accordingly, the prevalence of stage 3 AKI was significantly higher in the higher K^+ level groups than the lower K^+ level groups (χ^2=43.466, P<0.001). Significant interactions were also observed between serum K^+ and both 90-day mortality (χ^2 =29.113, P<0.001) and 1-year mortality (χ^2=27.696, P<0.001). The 90-day mortality in the six K^+ intervals from the lowest (<3.50 mmol/L) to the highest (≥5.50 mmol/L) were 28.3%, 21.9%, 30.1%, 35.4%, 45.2%, and 58.3%, respectively. The 1-year mortality rates in the six strata were 44.8%, 41.1%, 45.1%, 51.8%, 63.1%, and 76.3%, respectively.

Survival analysis

Of all patients, 263 (35.2%) died during the 90-day follow-up. Survival curves for 90-day all-cause mortality across categories of serum K^+ are presented in Figure 1. As shown in Table 2, among all cases of AKI-related mortality, 6.5% had K^+ levels <3.50 mmol/L, 8.0% had K^+ levels of 3.50–3.79 mmol/L, 17.5% had K^+ levels of 3.80–4.09 mmol/L, 36.9% had K^+ levels of 4.10–4.79 mmol/L, 17.9% had K^+ levels of 4.80–5.49 mmol/L, and 13.3% had K^+ levels ≥5.50 mmol/L.

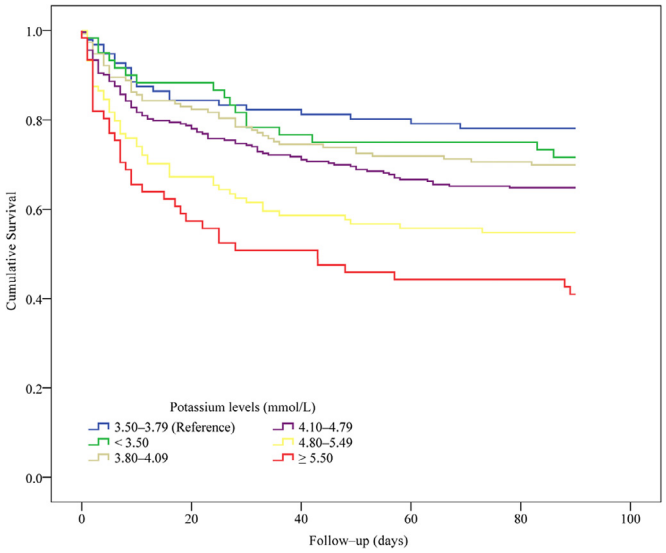

Figure 1. Kaplan–Meier plot of cumulative rates of 90-day mortality by serum potassium level (log-rank test: P<0.001).

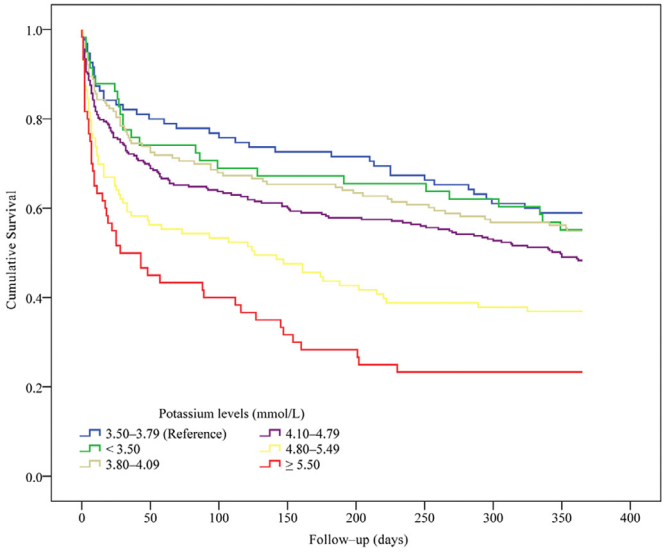

Figure 2. Kaplan–Meier plot of cumulative rates of 1-year mortality by serum potassium level (log-rank test: P<0.001).

During the 1-year follow–up, five patients were lost to follow-up, and 386 (52.0%) died. Survival curves for 1-year all-cause mortality across categories of the serum K^+ level are presented in Figure 2. Among patients who died, 6.7% of the cases had K^+ levels <3.50 mmol/L, 10.1% had K^+ levels of 3.50–

Table 2
Association of categories of the serum potassium level with 90-day and 1-year mortality.

K^+ levels (mmol/L)	90-day outcomes			1-year outcomes		
	Nonsurvivors (n=263, 35.2%)	Survivors (n=48, 464.8%)	P-value	Nonsurvivors (n=386, 52.0%)	Survivors (n=356, 48.0%)	P-value
<3.50	17 (6.5)	43 (8.9)	<0.001	26 (6.7)	32 (9.0)	<0.001
3.50–3.79	21 (8.0)	75 (15.5)		39 (10.1)	56 (15.7)	
3.80–4.09	46 (17.5)	107 (22.1)		69 (17.9)	84 (23.6)	
4.10–4.79	97 (36.9)	177 (36.6)		142 (36.8)	132 (37.1)	
4.80–5.49	47 (17.9)	57 (11.8)		65 (16.8)	38 (10.7)	
≥5.50	35 (13.3)	25 (5.2)		45 (11.7)	14 (3.9)	

Data are shown as n (%).

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*-value	HR	95% CI	*P*-value
MAP	0.971	0.962–0.980	<0.001	0.983	0.975–0.990	<0.001
Prealbumin	0.909	0.884–0.935	<0.001	0.914	0.896–0.933	<0.001
CRP	1.021	1.002–1.041	0.027	NA	NA	NA
MV	2.074	1.560–2.758	<0.001	2.069	1.650–2.594	<0.001
Na levels	1.027	1.014–1.040	<0.001	1.025	1.014–1.036	<0.001
K^+ levels (mmol/L)			<0.001			<0.001
3.50–3.79	Reference	Reference	Reference	Reference	Reference	Reference
<3.50	1.237	0.652–2.348	0.516	1.105	0.672–1.816	0.694
3.80–4.09	1.369	0.815–2.298	0.235	1.198	0.807–1.776	0.370
4.10–4.79	1.638	1.016–2.642	0.043	1.452	1.014–2.079	0.042
4.80–5.49	2.585	1.524–4.384	<0.001	2.151	1.427–3.241	<0.001
≥5.50	2.587	1.495–4.479	0.001	2.341	1.514–3.620	<0.001

CI: Confidence interval; CRP: C–reactive protein; HR: Hazard ratio; MAP: Mean arterial pressure; MV: Mechanical ventilation; NA: not available.

3.79 mmol/L, 17.9% had K^+ levels of 3.80–4.09 mmol/L, 36.8% had K^+ levels of 4.10–4.79 mmol/L, 16.8% had K^+ levels of 4.80–5.49 mmol/L, and 11.7% had K^+ levels ≥5.50 mmol/L.

In the multivariable-adjusted analysis, K^+ levels of 4.10–4.79 mmol/L (hazard ratio [HR]: 1.638, 95% confidence interval [CI]: 1.016–2.642, P=0.043); 4.80–5.49 mmol/L (HR: 2.585, 95% CI: 1.524–4.384, P<0.001); and ≥5.50 mmol/L (HR: 2.587, 95% CI: 1.495–4.479, P=0.001) were associated with 90-day mortality.

Significant interactions were also observed between serum K^+ levels and 1-year mortality in patients with K^+ levels of 4.10–4.79 mmol/L (HR: 1.452, 95% CI: 1.014–2.079, P=0.042); 4.80–5.49 mmol/L (HR: 2.151, 95% CI: 1.427–3.241, P<0.001); and ≥5.50 mmol/L (HR: 2.341, 95% CI: 1.514–3.620, P<0.001) [Table 3].

Discussion

Potassium is a ubiquitous cation contained mostly within the intracellular fluid. The serum K^+ concentration and the balance between the intra- and extracellular potassium concentrations play an important role in normal cell membrane electrophysiology. Dyskalemia is common in patients with AKI due to the central role of the kidneys in maintaining normal K^+levels. To our knowledge, 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 and 1-year mortality risk in relation to different serum K^+ intervals in very elderly patients with AKI. K^+ concentrations of 4.10–5.49 mmol/L and ≥5.50 mmol/L remain significant predictors of risk of death following multivariate adjustment. The K^+-mortality association is independent of AKI stage or use of beta-blockers and/or ACEI/ARB.[6] However, a K^+ level <3.50 mmol/L is typically not associated with increased mortality.

In the elderly, the incidence of electrolyte imbalance is known to be high because of organ decline, decreased physiologic reserves, frailty, and the higher prevalence of disability and functional impairment.[14–16] The kidneys are essential for maintaining homeostasis and are responsible for the reabsorption of water; AKI could magnify the effect of dyskalemia on the clinical consequences. Normal ranges of serum K^+ level within 3.50–5.50 mmol/L in clinical settings were determined mainly based on healthy subjects; hence, it is still unknown whether these values are applicable to elderly patients with complex comorbidities.[17] By interfering with tubular functions, AKI disturbs the physiologic regulation of electrolyte homeostasis, which could be more prominent in elderly individuals.

Recent studies have shown that optimal K^+ levels are different from those known previously. MacDonald and Struthers[1] examined the optimal K^+ levels in cardiovascular patients through a meta-analysis of four studies. They found that it is desirable to avoid hypokalemia and that the recommended serum K^+ level in patients with heart failure and myocardial infarction is 4.5–5.5 mmol/L. Nolan et al.[18] performed a retrospective study to suggest that a serum K^+ level of <4.4 mmol/L in patients with chronic heart failure was associated with an increased risk of sudden cardiac death; in their study, patients who survived the follow-up period had an average serum K^+ level of 4.4 ± 0.5 mmol/L, whereas those who died had an average serum K^+ level of 4.1 ± 0.6 mmol/L. Gao et al.[2] reported the results of a retrospective study that included 13,621 intensive care unit patients with AKI with a mean age of 65.3 years. They found that hypokalemia (<3.7 mmol/L) or hyperkalemia (≥4.8 mmol/L) in admitted patients was associated with the 90-day mortality. Our study results are consistent with those findings, further confirming that the significance of elevated serum K^+ levels is not limited to patients with cardiovascular disease or those needing critical care.

AKI with different conditions may require different management strategies. Critically ill patients often receive large volumes of fluids. Diuretics in such patients minimize fluid overload and may increase the urine output. However, diuretics may decrease the effective circulating volume or even aggravate kidney dysfunction and electrolyte imbalance. Generally, RRT is provided as a supportive treatment to AKI patients. The current KDIGO guidelines recommend initiation of RRT emergently if there are life-threatening complications of AKI, such as hyperkalemia or metabolic acidosis. However, in the absence of such complications, the appropriate timing for RRT initiation remains unclear. In the present study, we found that serum K^+ levels of 4.10–5.49 mmol/L and ≥5.50 mmol/L were associated with a significantly increased 90-day and 1-year risk of death in very elderly patients with AKI. Clinicians may not perform strict electrolyte management in such patients with serum K^+ levels ranging from 4.10 mmol/L to 5.49 mmol/L, because these AKI patients have normal K^+ levels. Our results have shown that even patients with normal serum K^+ levels can have increased

mortality. This reminds clinicians to evaluate other conditions throughout the body of very elderly patients with serum K^+ levels within the normal range, thereafter to optimize the treatment such as the timing for RRT. Therefore, further research should focus on serum K^+ and the prognosis of very elderly patients, with the establishment of new methods to assess the effective circulating volume.

The treatment and prevention of AKI remains a major challenge for intensive care physicians. Patients with AKI have impaired K^+ homeostasis. In the present study, we found that a serum K^+ level <3.50 mmol/L was not associated with increased mortality. This may be explained by several reasons. First, the mortality of patients with hypokalemia did not significantly change compared to patients with serum K^+ levels of 3.50–3.79 mmol/L in our study. The lower mortality rate among patients with hypokalemia suggests less statistical power to find a significant association. Second, patients with a serum K^+ level <3.50 mmol/L may be more easily recognized by practitioners, and timely treatment by clinicians can reduce the mortality to a certain extent. Of the 60 patients with serum K^+ level <3.50 mmol/L, half of them were treated with K^+ supplements. Third, patients with a K^+ level <3.50 mmol/L are not as ill as those with K^+ levels >3.5 mmol/L.

Our study has some limitations. First, subject selection bias cannot be ruled out, because the present study was retrospective in nature and most patients were retired elderly males, with only a few females having been treated. Second, we only analyzed serum K^+ levels on AKI diagnosis, and these levels could have changed over time (e.g., after initiating electrolyte therapy). In addition, factors that affected AKI prognosis were complicated, especially when the subjects were elderly people, with an average age of 87 years. 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 our results. Third, we used all-cause mortality but not cause-specific death.

Conclusions

Serum K^+ levels of 4.10–5.49 mmol/L and ≥5.50 mmol/L were associated with a significantly increased 90-day and 1-year mortality risk in very elderly patients with AKI. However, a serum K^+ level <3.50 mmol/L was not associated with increased mortality. Hence, controlling and maintaining the serum K^+ level within a safe range is critical in the clinical setting. Determining additional risk factors for AKI may be valuable and informative to clinicians for the identification of high-risk patients and for effective management of AKI.

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Ethical Approval

This study has been approved by the Ethics Committee of the Chinese PLA General Hospital (Number: S2017–054–01). The requirement for written informed consent was waived by the ethics committee of the designated hospital because this was an observational retrospective study.

Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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