

Serum Potassium and Outcomes in CKD: Insights from the RRI-CKD Cohort Study

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Background and objectives: The relationship between serum potassium (S_K) and mortality in chronic kidney disease (CKD) has not been systematically investigated.

Design, setting, participants, & measurements: We examined the predictors and mortality association of S_K in the Renal Research Institute CKD Study cohort, wherein 820 patients with CKD were prospectively followed at four US centers for an average of 2.6 years. Predictors of S_K were investigated using linear and repeated measures regression models. Associations between S_K and mortality, the outcomes of ESRD, and cardiovascular events in time-dependent Cox models were examined.

Results: The mean age was 60.5 years, 80% were white, 90% had hypertension, 36% had diabetes, the average estimated GFR was 25.4 ml/min per 1.73 m², and mean baseline S_K was 4.6 mmol/L. Higher S_K was associated with male gender, lower estimated GFR and serum bicarbonate, absence of diuretic and calcium channel blocker use, diabetes, and use of angiotensin-converting enzyme inhibitors and/or statins. A U-shaped relationship between S_K and mortality was observed, with mortality risk significantly greater at $S_K \leq 4.0$ mmol/L compared with 4.0 to 5.5 mmol/L. Risk for ESRD was elevated at $S_K \leq 4$ mmol/L in S_K categorical models. Only the composite of cardiovascular events or death as an outcome was associated with higher S_K (≥ 5.5).

Conclusions: Although clinical practice usually emphasizes greater attention to elevated S_K in the setting of CKD, our results suggest that patients who have CKD and low or even low-normal S_K are at higher risk for dying than those with mild to moderate hyperkalemia.

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Hyperkalemia (serum potassium [S_K] ≥ 5.5 mmol/L) is common in patients with ESRD. In the dialysis population, the prevalence of hyperkalemia has been estimated to range from 5 to 10% (1). Hyperkalemia is thought to contribute to 2 to 5% of deaths among patients with ESRD and accounts for up to 24% of emergency hemodialysis sessions in this population (2–4). Hyperkalemia has also been associated with increased mortality (up to 17%) in the general hospitalized population (5). Although nephron adaptation occurs in those with progressive renal insufficiency by way of enhanced distal tubular secretion of ingested potassium (6), mildly elevated potassium levels are not uncommon and dietary restriction of potassium is frequently considered prudent for patients with advanced chronic kidney disease (CKD) to avoid dangerous hyperkalemia (7).

Adverse effects of $S_K \leq 3.5$ mmol/L have been well docu-

mented in the cardiovascular literature. Among patients with heart failure, hypokalemia is associated with ventricular arrhythmias and death (8); however, little is known about adverse effects of hypokalemia in the CKD population, which is known to be at high risk for cardiovascular disease in general and sudden death in particular (9).

We postulated that lower (<3.5 mmol/L) levels of S_K would be associated with higher risk for mortality in a CKD population. The aims of this study were to examine the distribution and predictors of S_K and association, if any, of S_K with mortality, ESRD, the composite outcome of death or ESRD, and the composite of death or any cardiovascular event in a CKD cohort.

Materials and Methods

Data Source: The Renal Research Institute CKD Study

This prospective observational study of adult patients with stages 3 through 5 CKD was conducted at four outpatient nephrology clinics in the United States. Patients were recruited between June 2000 and February 2006. The inclusion criteria were age >18 years and a creatinine clearance of ≤ 50 ml/min by the Cockcroft-Gault formula, although subsequently estimated GFR (eGFR) values that were recalculated by the four-variable Modification of Diet in Renal Disease (MDRD) equation were occasionally >50 ml/min per 1.73 m². A total

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