

of CKD with availability of serum potassium in the majority of patients at multiple time points during follow-up, permitting analyses with  $S_K$  as a time-dependent covariate. The long duration of follow-up (median 3 years) and detailed medication data are additional strengths. Certain limitations merit consideration. Data on the dietary intake of potassium and protein was not collected in the Renal Research Institute CKD Study; however, we examined models with and without adjustment for serum albumin, a major marker of nutritional status. The predictive value of  $S_K$  was slightly attenuated by this adjustment, suggesting that nutritional state may be part of the explanation for the link between low  $S_K$  and mortality. In this study, death, ESRD, and cardiovascular event information was abstracted by study coordinators primarily from patient charts. It is possible that some events were not detected. The average time from the last  $S_K$  measure until death was 8.2 months, and the median was 5.8 months; therefore, we do not have values of  $S_K$  closer to the time of death.

The relatively weak association of higher  $S_K$  with mortality may be the result of dialysis initiation as “rescue” therapy in the face of emergent hyperkalemia and absence of data pertaining to serum potassium just proximate to dialysis initiation among those who reached ESRD. Similarly, the association between higher levels of  $S_K$  and cardiovascular events may reflect a survivor bias rather than a causal effect, although the latter cannot be excluded. Despite these limitations, the association, particularly at the lower end of the range of potassium levels in this patient population, could more plausibly be causally linked (based on what is known about the adverse effects of low potassium) to adverse outcomes in this and other patient populations. Causal inferences cannot be drawn with certainty, however, in the setting of an observational study such as ours.

## Conclusions

Lower  $S_K$  (even less than or equal to a “normal” level of 4.0 mmol/L) seems to predict mortality to a relatively greater degree compared with the risk associated with  $S_K \geq 5.5$  mmol/L. This study shows that the levels of  $S_K$  that are associated with lowest risk for mortality are between 4.1 and 5.5 mmol/L, which suggests that maintaining  $S_K$  in this range may potentially help optimize survival in patients with CKD. Practice patterns could potentially be adapted to supplement potassium (through dietary modification or pills) and avoid use of loop diuretics whenever possible. The benefits of potassium-sparing diuretics such as aldosterone receptor–blocking agents may be due in part to their ability to “normalize” serum potassium levels. Aldosterone is increasingly recognized to be important in the pathogenesis of CKD (37,38), and mineralocorticoid receptor blockade is an increasingly used strategy in lowering proteinuria with the potential of both slowing renal disease progression and lowering mortality. These issues warrant future studies that specifically address the role of potassium supplementation in determining outcomes and study the deliberate optimization of serum potassium levels by use of specific drugs in randomized trials. Overall, our findings suggest that attention should be paid to patients who have CKD and are at the lower ranges of  $S_K$  as well as those with elevated

serum potassium to prevent adverse outcomes such as mortality, ESRD, and cardiovascular events.

## Acknowledgments

This study was funded by the Renal Research Institute (New York, NY) and Amgen. R.S. is Principal Investigator and B.W.G. is a Co-Investigator in the Centers for Disease Control and Prevention’s National Chronic Kidney Disease Surveillance Project (MM-1149-0/10). Report contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.

The results from this analysis were presented in part as a poster (TH-PO918) at the annual meeting of the American Society Nephrology; Philadelphia, PA; November 2 through 4, 2008.

We are grateful to all study coordinators and participating patients at the following study sites: University of Michigan (Ann Arbor, MI), Albany Medical Center (Albany, NY), Metabolism Associates (New Haven, CT), and University of North Carolina, Chapel Hill (Chapel Hill, NC).

## Disclosures

None.

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