Dietary Potassium in Chronic Kidney Disease: Do Not Restrict the Evidence

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Dear Editors,

WITH INTEREST WE read the systematic review and meta-analysis by Morris et al.[1] which concluded that dietary potassium (K^+) restriction in patients with chronic kidney disease (CKD) is associated with a 0.22 mEq/L decrease in serum K^+ and 40% lower mortality hazard, but not with progression of CKD. However, we would like to raise 2 points of concern, including (1) a discrepancy between the results of the meta-analyses and the original studies and (2) an overestimation of the effect of dietary K^+ restriction on serum K^+.

The meta-analysis in which Morris et al. analyzed the association between urinary K+ excretion (U_K, as proxy for dietary K^+ intake) and mortality included 4 studies. The hazard ratios calculated from the studies by He et al.,[2] Leonberg-Yoo et al.,[3] and Eisenga et al.[4] were all <1 and therefore favored dietary K^+ restriction. All 3 original studies, however, reported the opposite association. Leonberg-Yoo et al. and Eisenga et al. showed that $U_K <$ reference was significantly associated with a greater risk of all-cause mortality (hazard ratios of 1.5-1.7 and >2, respectively).[3,4] He et al. used the lowest U_K quartile as reference and showed in the fully adjusted model that all-cause mortality was lower in all higher quartiles, although this was not statistically significant.[2]

The meta-analysis by Morris et al. on urinary K^+ and CKD progression showed a hazard ratio >1 for He et al. (favors no restriction) and <1 for Eisenga et al. (favors restriction). Again, the original studies showed the opposite association: He et al. showed that $U_K >$ reference increased the risk of CKD progression (hazard ratios 1.0-1.6),[2] whereas Eisenga et al. showed that $U_K <$ reference increased the risk of CKD progression (hazard ratios >3.4).[4] It is also unclear why some studies were excluded from this meta-analysis. The inclusion criteria reported "any stage CKD," but the analysis of the ONTARGET and TRANSCEND trials was not included, while this study also included a subgroup with eGFR <60 mL/min/1.73m^2.[5] Participants with CKD were also present in other cohorts with baseline eGFR 60-90 mL/min/1.73m^2 and albuminuria,[6] which would classify as CKD Stage G2 A1-A3. Another question is why studies using a spot urine K^+ to creatinine ratio or food frequency questionnaires to assess dietary K^+ intake were excluded. These considerations are relevant, because at present the majority of available studies shows that higher dietary K^+ is associated with better kidney outcomes.[7] A placebo-controlled, double-blind randomized clinical trial is currently investigating whether K^+ supplementation slows CKD progression.[8]

Our second concern is the time points that were selected to analyze the association between dietary K^+ and serum K^+. Morris et al. included 2 randomized controlled trials and found that restricted dietary K^+ intake (33 mEq/day) reduced serum K^+ by 0.22 mEq/L in comparison to "liberal" dietary K^+ intake (40 mEq/day). In both studies serum K^+ was measured at multiple time points, but only the time points with the greatest differences in serum K^+ were included in the meta-analysis. In the study by Arnold et al.,[9] the difference at 6 months was used (0.5 mEq/L), whereas at 24 months this difference was less prominent (0.2 mEq/L). In the study by Cockram et al.,[10] the difference in serum K^+ at day 22 was selected (-0.3 vs. -0.5 mEq/L), whereas no differences at days 8 and 15 were observed (0 vs. 0.1 and -0.4 vs. -0.3 mEq/L). A related question is how representative the 2 studies are for dietary K^+ intake, because one study used extremely low K^+ liquid diets,[10] whereas in the other study ~50% of subjects combined a low K^+ diet with K^+ binders, which also lower serum K^+.[9] Finally, the K^+ content of the diet that was classified as liberal intake was still 2-3 times lower than current recommendations. According to a cross-sectional analysis of 3,893 patients with CKD Stage G3b or G4, lowering dietary K^+ intake from 40 to 33 mEq/day would lower serum K^+ by only 0.02 mEq/L.[8] Similarly, Noori et al. [11] showed that in 224 hemodialysis patients, predialysis serum K^+ was only 0.1 mEq/L higher when comparing the lowest to the highest quartile of K^+ intake (23 vs. 88 mEq/day).

In conclusion, we challenge the conclusion by Morris et al. that dietary K^+ restriction is associated with a reduced risk of death in patients with CKD and conclude that the relationship between dietary K^+ and serum K^+ was overestimated.

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References

1. Morris A, Krishnan N, Kimani PK, Lycett D. Effect of dietary potassium restriction on serum potassium, disease progression, and mortality in chronic kidney disease: a systematic review and meta-analysis. *J Ren Nutr.* 2020;30:276-285.
2. He J, Mills KT, Appel LJ, et al. Urinary sodium and potassium excretion and CKD progression. *J Am Soc Nephrol.* 2016;27:1202-1212.
3. Leonberg-Yoo AK, Tighiouart H, Levey AS, Beck GJ, Sarnak MJ. Urine potassium excretion, kidney failure, and mortality in CKD. *Am J Kidney Dis.* 2017;69:341-349.
4. Eisenga MF, Kieneker LM, Soedamah-Muthu SS, et al. Urinary potassium excretion, renal ammoniagenesis, and risk of graft failure and mortality in renal transplant recipients. *The Am J Clin Nutr.* 2016;104:1703-1711.
5. Smyth A, Dunkler D, Gao P, et al. The relationship between estimated sodium and potassium excretion and subsequent renal outcomes. *Kidney Int.* 2014;86:1205-1212.
6. Araki S, Haneda M, Koya D, et al. Urinary potassium excretion and renal and cardiovascular complications in patients with type 2 diabetes and normal renal function. *Clin J Am Soc Nephrol.* 2015;10:2152-2158.
7. Gritter M, Rotmans JI, Hoorn EJ. Role of dietary K^+ in natriuresis, blood pressure reduction, cardiovascular protection, and renoprotection. *Hypertension.* 2019;73:15-23.
8. Gritter M, Vogt L, Yeung SMH, et al. Rationale and design of a randomized placebo-controlled clinical trial assessing the renoprotective effects of potassium supplementation in chronic kidney disease. *Nephron.* 2018;140:48-57.
9. Arnold R, Pianta TJ, Pussell BA, et al. Randomized, controlled trial of the effect of dietary potassium restriction on nerve function in CKD. *Clin J Am Soc Nephrol.* 2017;12:1569-1577.
10. Cockram DB, Hensley MK, Rodriguez M, et al. Safety and tolerance of medical nutritional products as sole sources of nutrition in people on hemodialysis. *J Ren Nutr.* 1998;8:25-33.
11. Noori N, Kalantar-Zadeh K, Kovesdy CP, et al. Dietary potassium intake and mortality in long-term hemodialysis patients. *Am J Kidney Dis.* 2010;56:338-347.