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Race, Serum Potassium, and Associations With ESRD and Mortality

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Abstract

Background—Recent studies suggest that potassium levels may differ by race. The basis for these differences and whether associations between potassium levels and adverse outcomes differ by race is unknown.

Study Design—Observational study.

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Setting & Participants—Associations between race and potassium as well as the interaction of race and potassium with outcomes were investigated in the Racial and Cardiovascular Risk Anomalies in Chronic Kidney Disease (RCAV) study, a cohort of US veterans (N=2,662,462). Associations between African ancestry and potassium were investigated in African Americans in the Atherosclerosis Risk in Communities (ARIC) Study (N=3,450).

Predictors—Race (African American vs non-African American) for cross-sectional analysis; serum potassium as a continuous variable (for longitudinal analysis).

Outcomes—For cross-sectional analysis: potassium level; for longitudinal analysis: mortality and end-stage renal disease (ESRD) via linkage with the Veterans Affairs Vital Status File and the US Renal Data System.

Results—The RCAV cohort was 18% African American (N=470,985). Potassium levels were, on average, 0.162 mmol/L lower in African Americans compared to non-African Americans, with differences persisting after adjustment for demographics, comorbidities, and potassium-altering medication use. In the ARIC study, higher African ancestry was related to lower potassium levels (-0.027 mmol/L per each 10% African ancestry). In both race groups, higher and lower levels of potassium were associated with mortality. Compared to a potassium of 4.2 mmol/L, the mortality risk associated with lower levels of potassium was lesser in African Americans vs non-African Americans, whereas mortality risk associated with higher levels was slightly greater. For ESRD, risk-relationships were weaker, with no difference by race.

Limitations—No data on potassium intake.

Conclusions—African Americans had slightly lower serum potassium levels than non-African Americans. Consistent associations between potassium and percent African ancestry may suggest a genetic component to these differences. Higher and lower serum potassium levels were associated with mortality in both racial groups.

Index words

race; serum potassium; African American; African ancestry; genetic risk factor; hypokalemia; hyperkalemia; racial differences; mortality; end-stage renal disease (ESRD); kidney disease

Potassium is one of the major intracellular cations and is essential for several important body functions in humans, such as maintaining normal neuromuscular functioning, preserving fluid volumes in cells, and regulating blood pH. Potassium levels outside of the range of normal have been associated with increased risk of all-cause and cardiovascular mortality as well as cardiac arrhythmias and end-stage renal disease (ESRD).¹⁻⁶

Recent studies suggest that, on average, African Americans have lower levels of serum potassium than European Americans.^{1,6} Some have posited that the difference may be explained by lower dietary potassium intake than European American individuals,⁷⁻⁹ but racial differences in other potassium-influencing factors, such as medication use and comorbid conditions, might also play a role. Alternatively, some have proposed biological differences by ethnicity.^{1,10} In this context, a recent study investigating markers of mineral metabolism reported that genetic African ancestry in African Americans correlated with fractional excretion of phosphorus.¹¹ One small study of persons with chronic kidney

disease (CKD) found that risk-relationships between potassium and adverse outcomes differed by race, potentially supporting a biological basis; however, sample size was limited.¹

In response to these uncertainties, we investigated the association of race with serum potassium concentration in two cohorts, the Racial and Cardiovascular Risk Anomalies in CKD (RCAV) study, a cohort of US veterans accessing healthcare, and the population-based Atherosclerosis Risk in Communities (ARIC) Study. We evaluated potential explanatory factors in the cross-sectional association between serum potassium and race in the RCAV cohort and, to assess the evidence for a genetic component, the association between percent African ancestry and serum potassium among African Americans in the ARIC Study. Finally, we investigated whether the longitudinal relationship between potassium and mortality and between potassium and ESRD differed by race in the RCAV cohort.

Methods

Data Source and Study Population

The RCAV cohort utilized data from the national Veterans Affairs (VA) Corporate Data Warehouse LabChem data files, which has been previously described.^{12,13} The original cohort consisted of all patients with estimated glomerular filtration rate (eGFR) over 60 ml/min/1.73 m² (calculated using the CKD-EPI [CKD Epidemiology Collaboration] creatinine equation¹⁵) measured October 1, 2004–September 30, 2006 (N=3,582,478).¹⁴ In the current study, we subset this population to the 2,894,950 US veterans with measured serum potassium and creatinine in the outpatient setting after 2007, with the aim of studying a more contemporary population with a greater prevalence of reduced eGFR.¹⁵ Index date was defined as the first concomitant creatinine and potassium measurement on or after January 1, 2007. We excluded 232,488 participants with missing vital status and demographic characteristics, leaving a final population size of 2,662,462.

Measurement of Exposure and Baseline Covariates

The primary exposure in the RCAV study was race (African American vs non-African American), which was determined by self-report and obtained from the VA Corporate Data Warehouse along with other demographic variables. Blood pressure was measured in outpatient encounters; baseline systolic and diastolic blood pressures were assessed as the mean level in the year prior to index date. Index date serum creatinine and demographic characteristics were used to calculate eGFR using the CKD-EPI creatinine equation.¹⁵⁻¹⁷ Body mass index (BMI) was defined as body weight (in kg) divided by the square of body height (in m). Urine albumin-creatinine ratio (ACR) was assessed from outpatient laboratory assessments over the same year prior to index date for a sensitivity analysis. Comorbidities—including hypertension; diabetes; history of coronary artery disease, cardiovascular disease, or peripheral artery disease; and history of congestive heart failure—were defined using a qualifying inpatient or outpatient ICD-9-CM code present prior to the index date, as previously described.⁷ Information on medication use, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), loop or thiazide diuretics,

potassium-sparing diuretics, β -blockers, and other antihypertensive medications, were extracted from VA Pharmacy dispensation records.¹⁸

Outcomes

The outcome variable for cross-sectional analysis was serum potassium obtained from the national VA Corporate Data Warehouse LabChem data files. Using the index value, serum potassium was defined as a continuous variable and as a categorical variable (hypokalemia, defined as serum potassium <3.5 mmol/L; hyperkalemia, defined as serum potassium \geq 5.5 mmol/L), in order to be consistent with existing literature.^{2,4,6} The outcomes of the survival analyses were mortality and ESRD (defined as participants on dialysis or with a kidney transplant), and were obtained from VA Vital Status File and the US Renal Data System. Due to a lag in the availability of linked data, the end date of follow-up for mortality and ESRD was Sep. 15, 2011.¹⁹

Statistical Analysis

Cross-sectional Associations Between Race and Potassium in RCAV—We used chi-square and t-tests to assess differences in categorical and continuous variables by African-American race. Kernel density plots were used to plot the distribution of index potassium levels in the population. We used linear regression and logistic regression to investigate the association between race and potassium levels as a continuous variable and categorical variables (hypokalemia and hyperkalemia), respectively. An unadjusted model included race as a single covariate. Progressively adjusted models were used in order to evaluate potential explanatory factors in the race-potassium association. The demographic-adjusted model included age and gender. The covariate-adjusted model additionally accounted for eGFR; systolic blood pressure; BMI; diabetes mellitus; history of coronary artery disease, cardiovascular disease, or peripheral artery disease; and history of congestive heart failure. The fully-adjusted model additionally adjusted for the use of ACE inhibitor or ARB medications, loop or thiazide diuretics, potassium-sparing diuretics, β -blockers, and any other anti-hypertensive medications. Interaction terms of race and loop/thiazide diuretics with serum potassium as well as race and ACE inhibitors or ARBs with serum potassium were tested in each of the models.

Cross-sectional Associations Between Percent African Ancestry and Potassium in ARIC—The ARIC study is a prospective epidemiologic study conducted in four US communities where 15,792 middle-aged participants were recruited at the baseline visit (1987-1989).²⁰ Associations between race and serum potassium levels were confirmed using kernel density plots in the 15,539 participants with non-missing serum potassium levels at the baseline visit. To assess whether racial differences in serum potassium levels might have a genetic basis, we used linear regression to evaluate the association between percent African ancestry and baseline serum potassium levels among the 3,450 African American participants who provided consent for genetic analyses and who had available serum potassium at the baseline visit. Percent African ancestry was estimated using ANCESTRYMAP with approximately 1350 markers informative for European versus African ancestry.^{21,22} We evaluated the association of African ancestry with serum potassium levels first in an unadjusted model and then with progressive adjustment for age

and gender, education level and family income, health characteristics (BMI, eGFR, diabetes mellitus, and history of cardiovascular disease), and individual potassium-altering medications, including loop and thiazide diuretics, ACE inhibitors (ARBs were not yet on the market in 1987), and β -blockers.

Longitudinal Associations Between Potassium and Adverse Outcomes by Race in RCAV—To evaluate whether the differences in serum potassium levels by race were reflected in different risk-relationships with adverse outcomes, we used Cox proportional hazards regression to evaluate the interaction between race and serum potassium with subsequent mortality and ESRD in the RCAV cohort. Serum potassium was modeled as a linear spline term with 5 knots at 3.5, 4, 4.5, 5, and 5.5 mmol/L, respectively. All covariates in the fully-adjusted model (age; sex; eGFR; systolic blood pressure; BMI; diabetes mellitus; history of coronary artery disease, cardiovascular disease, or peripheral artery disease; history of congestive heart failure; ACE inhibitor or ARB medications; loop or thiazide diuretics; potassium-sparing diuretics; β -blockers; and other anti-hypertensive medications) were included in models of this analysis. Figures were plotted with a potassium level of 4.2 mmol/L as the reference point within each race-group, so as to visually assess differences in risk-relationships, and interactions were evaluated as the ratio of the hazard ratios (HRs) at each 0.1 mmol/L of potassium comparing African Americans to non-African Americans. As a sensitivity analysis, we repeated this analysis for ESRD using death as a competing event and, for ESRD and death, among the 277,226 participants with available ACR to further adjust for urine ACR.

All analyses were done in Stata MP/14.1. Research protocols of the RCAV study were approved by the institutional review committees at the Memphis and Long Beach VA Medical Centers.¹² Research protocols of the ARIC study were approved by the institutional review committees at each participating institution.²⁰

Results

Baseline Characteristics

The RCAV study population included 2,662,462 participants with a mean age of 62 years (Table 1). Overall, 470,985 (18.0%) participants were African American and 167,995 (6.3%) participants were female. The mean serum potassium concentration of participants was 4.2 ± 0.4 (standard deviation) mmol/L, and the mean eGFR was 80 ± 18 ml/min/1.73 m². African American participants were younger, more often female, with slightly higher blood pressure and history of hypertension but lower history of cardiovascular disease. Potassium levels were lower among African Americans, with a greater proportion of potassium levels <3.5 mmol/L compared to in non-African Americans (5.4% versus 2.2%; $p < 0.001$) and a smaller proportion of potassium levels >5.5 mmol/L (0.35% versus 0.62%; $p < 0.001$) (Figure 1). The pattern was similar in the ARIC data (Figure S1, available as online supplementary material).

Association of Race and Potassium Level in RCAV

In cross-sectional analyses of potassium levels and race in the RCAV cohort, the difference between serum potassium level in African Americans versus non-African Americans was -0.162 (95% confidence interval [CI], -0.164 to -0.161) mmol/L on average (Table 2). This association was attenuated but remained significant after subsequent progressive adjustment for potential confounders (demographic-adjusted model, -0.140 [95% CI, -0.141 to -0.139] mmol/L difference; covariate-adjusted model, -0.134 [95% CI, -0.135 to -0.132] mmol/L difference; fully-adjusted model, -0.109 [95% CI, -0.110 to -0.107] mmol/L difference). There was a significant interaction of both race and diuretics and race and ACE inhibitor/ARB therapy with serum potassium: African Americans had a lower potassium associated with diuretic use compared to non-African Americans ($p < 0.001$), whereas non-African Americans had higher potassium associated with ACE inhibitor/ARB use ($p < 0.001$; Table S1).

When potassium was categorized as a binary variable reflecting hypo- or hyperkalemia, there were similar associations with race. African Americans had higher risk of hypokalemia and lower risk of hyperkalemia in all unadjusted and progressively adjusted models. For example, in unadjusted analysis, the odds ratio (OR) of having a potassium level < 3.5 mmol/L was 2.50 (95% CI, 2.46-2.54) in African-American versus non-African American participants; this association was only slightly attenuated to 1.87 (95% CI, 1.84-1.90) in the fully-adjusted model. Similarly, the ORs of hyperkalemia (serum potassium > 5 mmol/L) in African Americans compared to non-African Americans were 0.49 (95% CI, 0.48-0.51) when using serum potassium > 5 mmol/L as the threshold and 0.57 (95% CI, 0.54-0.60) when using > 5.5 mmol/L as the threshold; in the fully-adjusted model, the corresponding ORs were 0.59 (95% CI, 0.58-0.60) and 0.62 (95% CI, 0.59-0.66).

Association of Percent African Ancestry With Potassium Levels Among African Americans in ARIC

There were 3,450 African Americans available for genetic analysis in the ARIC study (Table 3). The mean age of these participants was 53.5 years, and the mean serum potassium concentration was 4.19 mmol/L. The median percent African ancestry was 84.8% (interquartile range, 77.9%-89.4%). In unadjusted analysis, each additional 10% of African Ancestry was significantly associated with a -0.0265 (95% CI: -0.0421 to -0.0109) mmol/L difference in serum potassium levels. This association persisted in all models, including those adjusted for income, education, comorbidities, and concomitant medications. For example, in the fully adjusted model, each additional 10% of African Ancestry was significantly associated with -0.0162 (95% CI, -0.0321 to -0.0002) difference in serum potassium levels.

Association of Potassium and Adverse Outcomes in RCAV

In the RCAV cohort, there were 7,850 ESRD events and 411,936 mortality events over a median of 5.9 years of follow-up. The risk-relationship between baseline potassium and mortality was fairly similar by race: both higher and lower levels of potassium were associated with higher risk of mortality, with lowest risk corresponding to potassium levels between 4 and 5 mmol/L (Figure 2). The risk gradient was higher for low levels of

potassium than high levels of potassium. Risk increases were slightly higher among African Americans compared to non-African Americans in the higher range of potassium and slightly lower in the lower range of potassium. Additional adjustment for albuminuria in the 277,226 participants with available measures did not qualitatively change the risk relationships (Figure S2).

Risk relationships between potassium and ESRD were weaker than those with mortality (Figure 3). Although there was a suggestion of a U-shaped relationship, with higher risk at both higher and lower levels of potassium, there was no discernible difference in relationship by race. Similar associations were seen when taking into account the competing risk of death (Figure S3) and in the subgroup with adjustment for albuminuria (Figures S4 and S5).

Discussion

Using two large, diverse cohorts, we found that, on average, African Americans had lower serum potassium values than non-African Americans, with a higher risk of hypokalemia and lower risk of hyperkalemia. These associations were independent of demographic characteristics, comorbid conditions, and potassium-altering medications. We also found an association between greater extent of African ancestry and lower serum potassium levels, supporting the notion of a genetic component to potassium homeostasis. Despite these differences, the risk relationships among potassium abnormalities, mortality, and ESRD were fairly similar by race. Indeed, the risk-relationship with mortality in the higher range of potassium was higher among African Americans compared to non-African Americans, suggesting that, contrary to previous reports,¹ there is no higher tolerance for hyperkalemia among African Americans. On the other hand, because African Americans tend to have lower potassium levels on average than other ethnic groups, more African Americans may benefit from routine potassium monitoring and supplementation, particularly when prescribed medications that lower potassium levels.

Our finding of lower potassium levels among African Americans is consistent with several previous studies of specific patient populations. A study of 1,227 patients with CKD reported that black race was significantly associated with 0.08-mmol/L lower serum potassium level, compared to non-black patients.¹ Other studies have linked black race to higher risk of hypokalemia and lower risk of hyperkalemia in populations with various comorbidities.^{2,23-25} Our results add to these efforts by evaluating potential confounding factors in the race-potassium association and also by assessing this association on the genetic level. With the caveat that African ancestry is a general marker that can also relate to social constructs such as diet, income and education level, the persistent association despite adjustment for multiple confounders suggests that differences in serum potassium levels may be due in part to genetic variability. The observed association with ancestry could represent a single locus with a large effect size, such as the Duffy group and white blood cell count,²⁶ or multiple variants with small effects, akin to the known genetic determinants of serum magnesium.^{27,28} This study might be followed by additional investigations into the specific genes associated with serum potassium levels, leading to new insight into the regulators of potassium homeostasis.

At steady-state, serum potassium levels are affected by potassium intake, intracellular potassium distribution, and potassium excretion. The human kidney is the primary driver of potassium homeostasis, and it has the ability to excrete very large amounts of potassium. This adaptability is thought important in maintaining adequate potassium levels in the prehistoric era, when typical diets may have contained up to 15 g of potassium per day.²⁹⁻³¹ Modern-day potassium intake is much less (range, 2-3 g per day for most Americans).³² Many studies have reported that urinary potassium excretion is lower in African Americans than other ethnicities, which may suggest lower potassium intake is a partial explanation for lower serum potassium level.³²⁻³⁶ However, a post-hoc analysis of the Dietary Approaches to Stop Hypertension (DASH) trial suggested lower urinary potassium excretion in African Americans compared to whites even during a controlled 30-day feeding period.³² Results were not consistent across randomized diets and serum potassium was not available in all participants, leaving uncertainty in interpretation. Other explanations for racial differences in serum potassium levels could involve differences in gastrointestinal absorption or renin-angiotensin-aldosterone system activation. Alternatively, responses to potassium-altering medications could differ by race, consistent with our cross-sectional findings. The latter results must be interpreted cautiously given that indications for treatment may vary by race given the presence of race-specific anti-hypertensive medication recommendations.³⁷

Abnormal serum potassium levels have been associated with mortality and other adverse outcomes in previous studies. In the population-based ARIC study, high levels of serum potassium were associated with mortality while low levels were associated with incident type 2 diabetes.^{23,25} In patients with CKD, both hypo- and hyperkalemia were associated with death, ESRD, and major adverse cardiovascular events.^{2,4} Postulated mechanisms include an increased risk of arrhythmias or an increased risk of fibrosis, with the latter particularly salient in hypokalemia.³⁸ To our knowledge, only one other study looked at the role of race in the potassium-outcome association. There, mortality was associated with low serum potassium levels regardless of race, and high serum potassium levels were associated with mortality only in white participants.¹ Our results were similar in the lower levels of potassium but reverse in higher levels of potassium, demonstrating instead that high serum potassium levels were associated with higher risk of death in African American participants compared to non-African Americans. Given the relative rarity of hyperkalemia among African American participants, power may have been limited in the previous study, which had a much smaller sample size. The interaction with race observed in our study may reflect the differences in baseline distribution of potassium, with risk corresponding to deviations from a baseline value rather than a certain threshold value.

There are certain strengths and limitations to our study. The VA population is large and nationally representative of US veterans, providing sufficient power for our analyses. Racial differences in socioeconomic status and access to care are likely smaller in this population than in the unselected general population. In the ARIC study, we evaluated the relationship not only between potassium and self-reported race, which may represent more of a social construct, but also between potassium and percent African ancestry determined from genetic admixture analysis. As a limitation, however, there were no data on potassium intake or urinary excretion of potassium, both potentially important confounders in the association of race and serum potassium level. Also, ancestry-informative markers vary considerably

among different African American subgroups, and results of our genetic analysis may not be generalizable to all African American subgroups.¹¹ Finally, over 90% of the VA population were men; therefore, our results detailing the longitudinal relationship between potassium and the risk of mortality and ESRD may be less applicable to women.

In summary, we found that African Americans had lower serum potassium levels than non-African Americans in two large cohorts, and we demonstrated that greater percent African ancestry was associated with lower serum potassium. Both hypokalemia and hyperkalemia were risk factors for mortality, and African Americans had slightly higher risk in hyperkalemia and slightly lower risk in hypokalemia compared to non-African Americans. Contrary to previous studies, these results suggest that potassium monitoring may require even greater vigilance among African Americans, particularly when they begin receiving potassium-wasting medications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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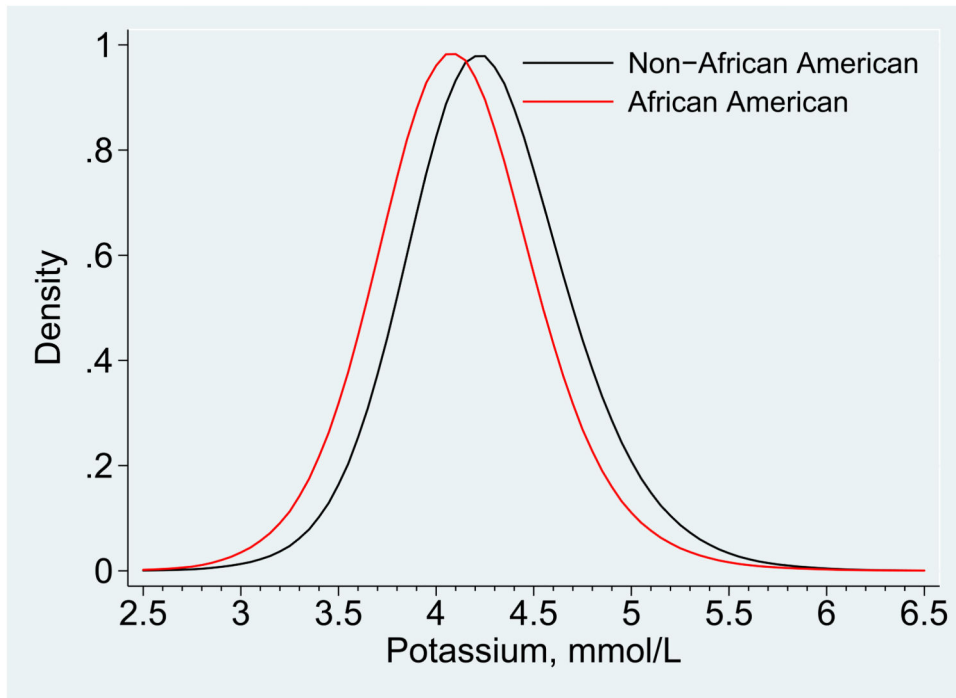


Figure 1. Distribution of potassium levels in the Racial and Cardiovascular Risk Anomalies in Chronic Kidney Disease (RCV) cohort, by race (N=2,662,462)

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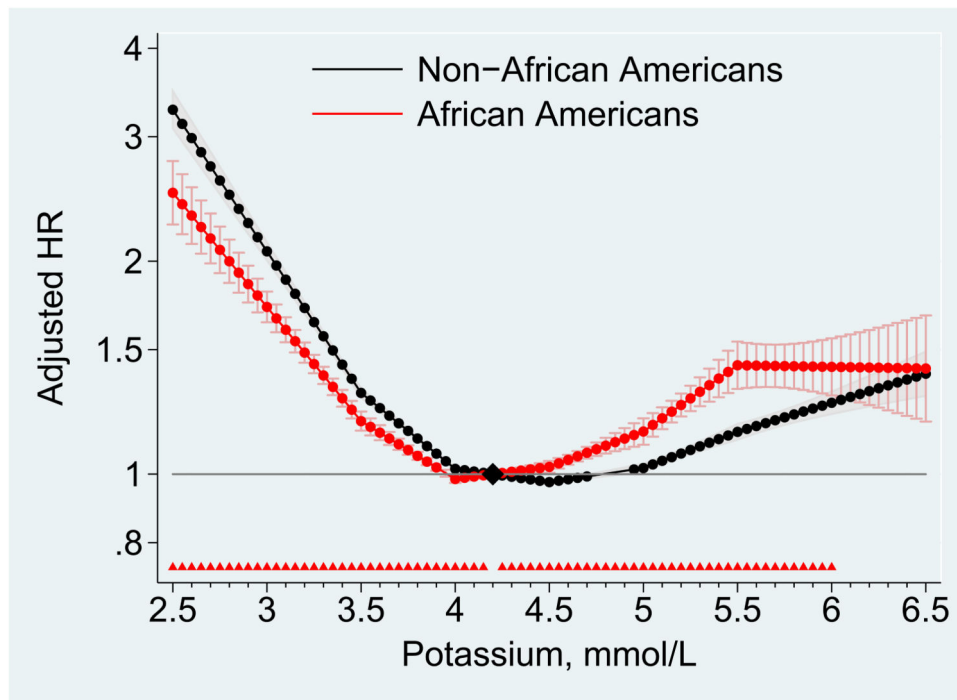


Figure 2.

Adjusted association between baseline potassium level and all-cause mortality, stratified by race.

*Reference point (black diamond) is 4.2 mmol/L within African Americans and within non-African Americans. Bold dots represent point estimates that are significant different than 1; brackets represent the 95% confidence interval. Red stars along the x-axis represent significant point-wise interaction, comparing the adjusted hazard ratio of the potassium value to 4.2 mmol/L between African Americans and non-African Americans. Potassium is represented as a series of linear splines with knots at 3.5, 4, 4.5, 5, and 5.5 mmol/L.

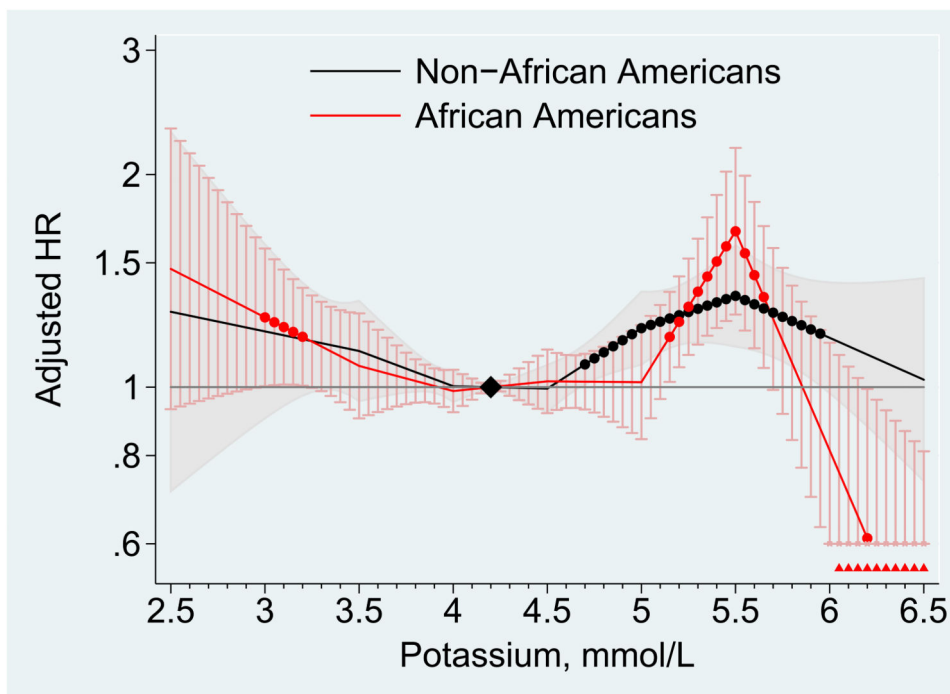


Figure 3.

Adjusted association between baseline potassium level and end-stage renal disease, stratified by race.

* Reference point (black diamond) is 4.2 mmol/L within African Americans and within non-African Americans. Bold dots represent point estimates that are significant different than 1; brackets represent the 95% confidence interval. Red stars along the x-axis represent significant point-wise interaction, comparing the adjusted hazard ratio of the potassium value to 4.2 mmol/L between African Americans and non-African Americans. Potassium is represented as a series of linear splines with knots at 3.5, 4, 4.5, 5, and 5.5 mmol/L.

Table 1
Baseline characteristics of the RCAV study population, by ethnicity

	Overall (N=2,662,462)	Non-African American (n=2,191,477 [82%])	African American (n=470,985 [18%])
Age, y	62 (13)	63 (13)	57 (12)
Female sex	167995 (6.3%)	121143 (5.5%)	46852 (10%)
Potassium, mmol/L	4.2 (0.4)	4.3 (0.4)	4.1 (0.4)
Diabetes mellitus	712293 (27%)	580800 (27%)	131493 (28%)
Diagnosed hypertension	1754223 (66%)	1432092 (65%)	322131 (68%)
History of CAD, CVD, or PAD	773624 (29%)	679765 (31%)	93859 (20%)
History of CHF	129724 (4.9%)	107621 (4.9%)	22103 (4.7%)
ACE inhibitor or ARB use	898966 (34%)	753711 (34%)	145285 (31%)
Thiazide or Loop Diuretic use	561417 (21%)	441683 (20%)	119734 (25%)
Potassium-sparing Diuretic use	99979 (3.8%)	76812 (3.5%)	23167 (4.9%)
B-blocker use	690957 (26%)	591616 (27%)	99341 (21%)
Other antihypertensive medication use	725370 (27%)	579305 (26%)	146065 (31%)
Systolic BP, mmHg	132 (17)	131 (17)	133 (18)
Diastolic BP, mmHg	76 (11)	75 (11)	79 (12)
BMI, Kg/m ²	29 (6)	30 (6)	29 (6)
eGFR, ml/min/1.73m ²	80 (18)	78 (17)	87 (20)
ACR, mg/g	11 [5-33]	11 [5-33]	10 [4-32]

Note: Values for categorical variables are given as percentages; values for continuous variables, as mean \pm standard deviation or median [interquartile range]. For all rows except ACR, $P < 0.001$.

ACE, angiotensin-converting enzyme; ACR, albumin-creatinine ratio; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CHF, congestive heart failure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; PAD, peripheral artery disease; RCAV, Racial and Cardiovascular Risk Anomalies in Chronic Kidney Disease

Table 2
Association of ethnicity with serum potassium in progressively adjusted models

Model	Mean Difference in Potassium, AA vs non-AA, mmol/L	OR for Hypokalemia: Potassium <3.5 mmol/L	OR for Hyperkalemia	
			Potassium >5 mmol/L	Potassium 5.5 mmol/L
1	-0.162 (-0.164 to -0.161)	2.50 (2.46-2.54)	0.49 (0.48-0.51)	0.57 (0.54-0.60)
2	-0.140 (-0.141 to -0.139)	2.39 (2.35-2.43)	0.56 (0.55-0.58)	0.66 (0.62-0.70)
3	-0.134 (-0.135 to -0.132)	2.28 (2.24-2.32)	0.55 (0.53-0.58)	0.59 (0.56-0.63)
4	-0.109 (-0.110 to -0.107)	1.87 (1.84-1.90)	0.59 (0.58-0.61)	0.62 (0.59-0.66)

Note: Associations in first column given as β coefficient (95% confidence interval) and in other columns as odds ratio (95% confidence interval). The first column reflects the mean difference in potassium levels for African Americans compared to non-African Americans; the following three columns reflect the odds for the column label (e.g., hypokalemia) for African Americans compared to non-African Americans. Model 1 is unadjusted. Model 2 adjusts for age and sex. Model 3 adjusts for age; sex; estimated glomerular filtration rate; systolic blood pressure; body mass index; diabetes mellitus; history of coronary artery disease, cerebrovascular disease, or peripheral artery disease; and history of heart failure. Model 4 adjusts for all of the aforementioned covariates as well as the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, thiazide or loop diuretics, potassium-sparing diuretics, β -blockers, and other anti-hypertensive medications. OR, odds ratio, AA, African American

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Table 3
Association of African ancestry with serum potassium in progressively adjusted models among African-American participants in ARIC Study

	Potassium, mmol/L, per 10% greater African ancestry
Model 1	-0.0265 (-0.0421 to -0.0109)
Model 2	-0.02668 (-0.0421 to -0.0113)
Model 3	-0.0212 (-0.0382 to -0.0042)
Model 4	-0.0239 (-0.0391 to -0.0086)
Model 5	-0.0196 (-0.0364 to -0.0028)
Model 6	-0.0162 (-0.0321 to -0.0002)

Note: n=3450. Model 1 is unadjusted; model 2 adjusts for age and sex; model 3 adjusts for age, sex, income and education level; model 4 adjusts for age, sex, estimated glomerular filtration rate; body mass index, diabetes mellitus, and history of cardiovascular disease; model 5 adjusts for all of the aforementioned covariates; model 6 adjusts for model 5 as well as diuretics, angiotensin-converting enzyme inhibitors, and β -blockers. ARIC, Atherosclerosis Risk in Communities

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