

Potassium and Glucose Measures in Older Adults: The Cardiovascular Health Study

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Background. We sought to determine the impacts of serum and dietary potassium measures on glucose metabolism and diabetes risk in older adults.

Methods. Among participants of the Cardiovascular Health Study, a community-based cohort of older American adults, we examined a) cross-sectional associations between potassium and measures of insulin sensitivity and secretion estimated from oral glucose tolerance tests and b) longitudinal associations of serum and dietary potassium with diabetes risk.

Results. Among 4,754 participants aged ≥ 65 years at baseline, there were 445 cases of incident diabetes during a median follow-up of 12 years. In multivariate models, baseline serum and dietary potassium were both associated with lower insulin sensitivity and greater insulin secretion. Compared with those with a serum potassium ≥ 4.5 mEq/L, participants with a serum potassium < 4.0 mEq/L had an adjusted mean difference in Matsuda insulin sensitivity index of -0.18 ($-0.39, 0.02$). Compared with those in the highest quartile, participants in the lowest quartile of dietary potassium intake had a corresponding adjusted mean difference in Matsuda insulin sensitivity index of -0.61 ($-0.94, -0.29$). In multivariate models, neither serum nor dietary potassium intake was associated with long-term diabetes risk.

Conclusions. Although we did not identify serum and dietary potassium as risk factors for incident diabetes in older adults, results from cross-sectional analyses suggest that both may be associated with increased insulin resistance. This relationship with insulin resistance needs to be confirmed, and its importance on diabetes risk, cardiovascular risk, and conditions specific to older adults should be determined as well.

Key Words: Potassium—Glucose metabolism—Older adults.

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ALTHOUGH prevention and treatment of obesity are the primary means of diabetes prevention in a general population, weight loss may not be advisable for all older adults. Identifying and addressing other potentially remediable risk factors may be more desirable for this population. Serum and dietary potassium are novel, potentially modifiable risk factors for diabetes. Low serum potassium has been studied as a risk factor in the context of diuretic use. Mixed associations have been reported, with some (but not all) studies finding potassium to be a significant mediator

of the association between thiazide use and increased diabetes risk (1–5). Recent prospective studies have found lower serum potassium to be associated with higher risk of type 2 diabetes independent of thiazide diuretic use (6,7). Low dietary potassium intake has also been identified as a diabetes risk factor, particularly in African Americans (8). Although in vitro studies and glucose clamps in healthy volunteers have attempted to clarify the effects of potassium on glucose metabolism (9–13), the associations between low potassium and measures of glucose metabolism have

not been clearly elucidated in larger cohorts. Moreover, these associations have not been thoroughly examined in older adults who have the highest prevalence of diabetes and hypertension, who are recommended to take diuretics as first-line therapy for hypertension, and who may develop diabetes through different metabolic pathways compared with younger adults (14–16). To assess the cross-sectional associations of potassium with measures of glucose metabolism, including insulin sensitivity and secretion and to examine the importance of potassium on diabetes risk in older adults, we studied participants enrolled in the Cardiovascular Health Study (CHS), a population-based cohort of older Americans who have been followed for over two decades.

METHODS

CHS is a prospective, community-based cohort of adults of ≥ 65 years of age. Initial recruitment consisted of 5,201 participants in 1989–1990; subsequently, an additional 687 predominantly African American participants were recruited in 1992–1993. Participants were recruited from Medicare eligibility lists from four US communities: Forsyth County, North Carolina, Sacramento County, California, Washington County, Maryland, and Allegheny County, Pennsylvania. Exclusion criteria for CHS included active treatment for cancer, inability to provide personal informed consent, and use of a wheelchair within the home. After the initial in-person baseline exam, patients were contacted semiannually and came annually for in-person visits through 1999 and by semiannual telephone call alone through the present except for an additional visit in 2005–2006. Institutional review boards at each of the participating institutions approved the study, and written informed consent was obtained from each participant.

Exclusions

Cross-sectional: Because the African American cohort did not undergo a baseline 2-hour oral glucose tolerance test (OGTT), we used data from the initial cohort of 5,201 participants for cross-sectional analyses, excluding participants with prevalent diabetes ($n = 763$), missing information on diabetes status at baseline ($n = 61$), missing or inadequate fasting state ($n = 254$), outlying insulin level ($n = 1$), or missing data for glucose or insulin measures ($n = 169$). Our final study sample for cross-sectional analyses included 3,953 participants.

Longitudinal: For our longitudinal analyses of serum potassium and diabetes risk, we excluded participants sequentially from the analysis if they had prevalent diabetes ($n = 925$), defined as fasting glucose ≥ 126 mg/dL (6.99 mmol/L), nonfasting glucose ≥ 200 mg/dL (11.1 mmol/L), or use of diabetes medications, or were missing information about diabetes status from the baseline

exam ($n = 98$); or if they had no data on diabetes status at any of the follow-up exams ($n = 111$). Our final study sample consisted of 4,754 participants for these longitudinal analyses.

Longitudinal analyses of dietary potassium and diabetes risk were limited to the participants from the initial cohort of 5,201 participants; the African American cohort did not complete a diet assessment at baseline. After additionally excluding those with missing dietary information ($n = 140$) and implausibly low and high values of total caloric intake (<500 kcal/d or $>5,000$ kcal/d) ($n = 35$), dietary analyses included 4,111 participants.

Outcomes

For the cross-sectional analyses, there were three main outcomes of interest based on the OGTT done at baseline: (a) insulin sensitivity using the Matsuda insulin sensitivity index (Matsuda ISI); (b) insulin sensitivity using the Gutt index; and (c) insulin secretion using a β -cell function index. All three of these indices utilize measures of glucose and insulin at 0 and 120 minutes during the OGTT (17–19). Two-hour glucose and fasting insulin measures were also examined as outcomes for these analyses.

The outcome for the longitudinal analyses was incident type 2 diabetes defined as a fasting glucose ≥ 126 mg/dL (6.99 mmol/L), nonfasting glucose ≥ 200 mg/dL (11.1 mmol/L), or use of diabetes medications. Validated medication inventories were performed annually. Glucose was measured at examinations in 1989–1990, 1992–1993, 1994–1995, 1996–1997, and 1998–1999; all were fasting except 1994–1995. Incident diabetes was ascertained through 2006.

Exposures

Serum potassium was measured at the 1989–1990 and 1992–1993 exams, after standard collection and storage, using the Kodak Ektachem 700 Analyzer (Eastman Kodak, Rochester, New York), a colorimetric method (20). Coefficients of variation for serum potassium measurements were approximately 2% (16). We categorized serum potassium into categories based on clinically relevant cut points of <4.0 , 4.0 – <4.5 , and ≥ 4.5 mEq/L. Dietary potassium was assessed at the 1989–1990 examination using a validated block food-frequency questionnaire administered with picture cards, sorted by frequency of use (21,22). We categorized dietary potassium into quartiles.

Covariates

For the cross-sectional and longitudinal analyses of the association between serum potassium and measures of glucose metabolism or diabetes risk, we included the following as covariates: age, race (black, nonblack), sex, clinic site, body mass index (BMI), waist circumference, physical

activity (the weighted sum of kilocalories expended in self-reported physical activities) (23), smoking (never, former, current), alcoholic drinks per week (0, <7, 7+), systolic blood pressure, and use of angiotensin-converting enzyme inhibitors (ACE-I), beta blockers, and diuretics. For cross-sectional and longitudinal analyses of the association between dietary potassium and diabetes risk or glucose metabolism, we included all of the above covariates as well as dietary score (which reflects intake of foods with high dietary fiber, low glycemic index, trans fat, and higher ratio of polyunsaturated/saturated fat in diet) (24), and total energy intake. Renal function, at baseline, measured as cystatin-based glomerular filtration rate (eGFR_{cys}), was also examined as a potential covariate (25).

Statistical Analyses

We calculated the mean and standard deviation or frequency of baseline characteristics of the study population by category of serum potassium (<4.0, 4.0-4.5, and ≥ 4.5 mEq/L). We used multivariable linear regression models for the cross-sectional analyses of the associations between both serum and dietary potassium, as continuous and categorical variables, and measures of insulin resistance and insulin secretion. To evaluate the reliability of serum potassium measurements, we used a one-way random effects model to calculate the interclass correlation coefficient among $n = 3,533$ participants who had repeated measures of serum K at years 2 and 5, and whose diuretic use did not change between exams. We used multivariate Cox proportional hazard regression models for our longitudinal analyses of the associations of serum and dietary potassium, as continuous and categorical variables, with risk of incident diabetes, adjusting for the covariates described earlier. For serum potassium, we fit time-varying model using a cumulative average to update potassium values. To evaluate whether the associations varied with shorter follow-up time, we truncated follow-up at 5 years in a sensitivity analysis. For both cross-sectional and longitudinal analyses, we assessed for possible interaction between potassium (serum or dietary) with age, sex, race, and diuretic use by including cross-product terms in the regression models. We performed stratified analyses by diuretic-use status.

All p -values were two sided, and a p -value of <.05 was considered to be statistically significant. All statistical analyses were conducted using Stata software version 11.2 (StataCorp, College Station, Texas).

RESULTS

Table 1 describes the baseline characteristics of participants by category of serum potassium. The highest category of serum potassium (≥ 4.5 mEq/L) was significantly associated with higher age, lower BMI, greater physical activity,

lower insulin and systolic blood pressure levels, lower use of diuretics, and lower dietary potassium intake. There was a higher percentage of blacks (21%) among those in the lowest category of serum K (<4.0mEq/L) compared with the other categories of serum K.

Cross-Sectional Analyses of Measures of Glucose Metabolism

Among the 3953 participants included in the cross-sectional analyses of serum potassium and measures of glucose metabolism, the mean (SD) of the 2-hour glucose and fasting insulin baseline levels for the cohort were 137.5 mg/dL (42.3) [7.63 mmol/L (2.35)] and 13.7 IU/mL (6.9) [95.15 pmol/L (47.92)], respectively. The mean (SD) values for measures of insulin sensitivity and insulin secretion for the cohort were as follows: Matsuda ISI: 3.6 (2.3), Gutt index: 61.0 (23.8), and β -cell function index: 1,381.8 pmol/L (587.9).

In multivariate models adjusting for age, race, sex, clinic site, BMI, waist circumference, physical activity, smoking, alcohol use, systolic blood pressure, and use of ACE-I, beta blockers, and diuretics, participants with a serum potassium of <4.0 and 4.0-4.5 mEq/L had higher 2-hour glucose, higher fasting insulin, lower Matsuda ISI, lower Gutt index, and statistically significantly higher β -cell function index levels (p values of trend were .22, .58, .08, .07, and .03, respectively) compared with those with a serum potassium ≥ 4.5 mEq/L (Table 2).

In multivariate models adjusting for the aforementioned covariates, diet score, and total energy intake, participants in the lower quartiles of dietary potassium had higher 2-hour glucose ($p_{\text{trend}} = .24$) and higher fasting insulin measures ($p_{\text{trend}} = .07$). Lower dietary potassium was significantly associated with lower Matsuda ISI, lower Gutt index, and higher β -cell function index levels, with p values of trend of <.001, .001, and .007, respectively (Table 3). Further adjustment for renal function, as measured by eGFR_{cys}, had no appreciable effect on these cross-sectional findings. We found no statistically significant interactions between serum or dietary potassium and diuretic use for any of the measures of glucose metabolism.

For analyses of both serum and dietary potassium, we found a similar pattern of associations among participants who were not on any diuretics.

Longitudinal Analyses of Diabetes Risk

Among the 4,754 participants included in longitudinal analyses of serum potassium and diabetes risk, mean serum potassium was 4.2mEq/L. During a median of 11.6 years of follow-up, there were 445 cases of incident diabetes, with crude incident rates of diabetes of 9.1, 8.4, and 8.0 cases per 1,000 person years for those participants with a serum potassium of <4.0, 4-4.5, and ≥ 4.5 mEq/L, respectively.

Table 1. Characteristics of CHS Participants at Baseline by Serum Potassium

Characteristic	Serum Potassium (mEq/L)			p Value
	<4.0	4-4.5	≥4.5	
No. of participants	1,215	2,549	990	
Serum potassium (mEq/L)	3.70±0.22	4.20±0.13	4.66±0.19	
Age (y)	72.6±5.3	72.4±5.4	73.7±6.1	<.001
Male	362 (29.8%)	1,040 (40.8%)	538 (54.3%)	<.001
Black	260 (21.4%)	279 (10.9%)	91 (9.2%)	<.001
BMI (kg/m ²)	26.8±4.9	26.3±4.5	25.7±4.2	<.001
Waist (cm)	93.7±13.3	93.2±12.9	93.0±12.3	.34
Systolic BP (mm Hg)	138.6±22.0	134.8±21.6	134.1±21.1	<.001
Hypertension medication	811 (66.7%)	922 (36.2%)	343 (34.6%)	<.001
Beta blocker	156 (12.8%)	286 (11.2%)	134 (13.5%)	.11
ACE-I	86 (7.1%)	125 (4.9%)	77 (7.8%)	.001
Diuretic	595 (49.0%)	436 (17.1%)	122 (12.3%)	<.001
Thiazide diuretics without k-sparing agents	323 (26.6%)	140 (5.5%)	31 (3.1%)	<.001
Thiazide diuretics with k-sparing agents	190 (15.6%)	158 (6.2%)	41 (4.1%)	<.001
Loop diuretics	75 (6.2%)	133 (5.2%)	47 (4.7%)	.30
CHD	213 (17.5%)	413 (16.2%)	201 (20.3%)	.02
CHF	52 (4.3%)	72 (2.8%)	40 (4.0%)	.04
C-reactive protein (mg/L)	4.6±6.6	4.0±6.4	4.6±8.8	.009
eGFR _{cys}	78.9±19.8	79.7±18.4	73.9±19.2	<.001
HDL (mg/dL)	57.0±16.9	55.6±15.6	53.7±15.3	<.001
LDL (mg/dL)	127.6±34.8	131.8±35.2	131.3±34.1	.002
Triglycerides (mg/dL)	134.1±71.2	133.0±64.4	133.2±67.6	.89
Glucose (mg/dL)	100.0±10.6	99.1±9.5	100.0±9.4	.01
Insulin (IU/mL)	14.5±7.9	13.6±11.7	13.4±6.5	.01
Physical activity (kcal/wk)	1,637±1843	1,817±2117	1,901±2,189	.007
Self-reported health				
Excellent	147 (12.1%)	412 (16.2%)	162 (16.4%)	<.001
Very good	278 (23.0%)	673 (26.4%)	270 (27.3%)	
Good	459 (37.9%)	965 (37.9%)	351 (35.5%)	
Fair	269 (22.2%)	441 (17.3%)	179 (18.1%)	
Poor	57 (4.7%)	55 (2.2%)	26 (2.6%)	
Smoking status				
Never	626 (51.5%)	1,190 (46.7%)	402 (40.6%)	<.001
Former	455 (37.4%)	1,050 (41.2%)	452 (45.7%)	
Current	134 (11.0%)	309 (12.1%)	136 (13.7%)	
Alcohol (drinks/wk)				
None	642 (52.8%)	1,112 (43.6%)	451 (45.6%)	<.001
<7	438 (36.0%)	1,025 (40.2%)	376 (38.0%)	
7+	135 (11.1%)	412 (16.2%)	163 (16.5%)	
Dietary potassium*	3,334±1,118	3,307±1,099	3,216±1,076	.02
Diet score*	0.47±0.50	0.46±0.50	0.42±0.49	.07

Notes: ACE-I = angiotensin-converting enzyme inhibitor; BMI = body mass index; BP = blood pressure; CHD = cardiovascular heart disease; CHS = Cardiovascular Health Study; CHD = cardiovascular heart disease; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; LDL = low density lipoprotein.

*Available only among participants enrolled in 1989–1990. Diet score between 1 and 5 corresponding to a value related to the sum of participant's quintile of intake of foods with high dietary fiber, low glycemic index, trans fats, high polyunsaturated-to-saturated fat ratio (24).

Among the 4,111 participants included in the longitudinal analyses of dietary potassium and diabetes risk, the mean dietary potassium was 3,191 mg/d. The correlation between serum and dietary potassium was $-.04$ ($p = .02$) and partial correlation coefficients accounting for any one of age, sex, diuretic use, or energy intake were similar. During a median follow-up time of 12.1 years, there were 375 cases of incident diabetes, with crude incident rates of diabetes of 9.8, 6.9, 8.7, and 7.2 cases per 1,000 person years for those participants with the lowest to highest quartiles of dietary potassium intake.

There was no significant association between serum potassium and risk of diabetes in minimally or fully adjusted models.

Compared with participants in the highest serum K category, those in the lowest category had an adjusted hazard ratio (HR) (95% confidence interval [CI]) of 0.98 (0.72, 1.32) (Table 4). There were no significant associations between serum potassium and risk of diabetes in the short term, at the end of 5 years of follow up. There were no statistical interactions between serum potassium and age ($p = 1.0$), sex ($p = .60$), race ($p = .64$), or diuretic use ($p = .23$). The intraclass correlation coefficient calculated among CHS participants with repeated serum potassium measures 3 years apart was .45.

In minimally adjusted models, adjusted only for age, sex, race, and clinical site, we found a significant association

Table 2. Associations of Serum Potassium Concentration With Measures of Glucose Tolerance, Insulin Sensitivity, and Insulin Secretion Among CHS Participants Enrolled During 1989–1990 (n = 3,953)

Measure	Adjusted Mean Difference in Measure by Serum Potassium Concentration* (mEq/L)				Per Standard Deviation Decrease [†]
	<4.0	4-<4.5	≥4.5	<i>p</i> _{trend}	
2-h glucose (mg/dL)	2.4 (-1.6, 6.5)	3.4 (.1, 6.6)	Ref.	.22	0.86 (-0.54, 2.26)
Fasting insulin (IU/mL)	0.19 (-.42, 0.80)	-.20 (-0.69, 0.28)	Ref.	.58	0.05 (-0.16, 0.26)
Matsuda ISI	-.18 (-0.39, 0.02)	-.11 (-0.28, 0.05)	Ref.	.08	-0.06 (-0.13, .02)
Gutt index	-1.99 (-4.19, 0.22)	-1.99 (-3.75, -0.23)	Ref.	.07	-0.58 (-1.35, 0.18)
Stumvoll β-cell function index (pmol/L)	63.4 (7.9, 118.9)	2.6 (-41.6, 46.9)	Ref.	.03	19.7 (0.45, 39.0)

Notes: *Adjusted for age, race (black, nonblack), sex, clinic site, body mass index, waist circumference, physical activity, smoking (never, former, current), alcoholic drinks per week (0, <7, 7+), systolic blood pressure, angiotensin-converting enzyme inhibitor use, beta-blocker use, diuretic use.

[†]Standard deviation of potassium = 0.37 mEq/L.

Table 3. Association of Dietary Potassium Intake With Measures of Glucose Tolerance, Insulin Sensitivity, and Beta-Cell Function Among CHS Participants Enrolled During 1989–1990 (n = 3,730)

Measure	Adjusted Mean Difference in Measure by Dietary Potassium Concentration* (mg/d)				<i>p</i> _{trend}	Per Standard Deviation Decrease [†]
	≤2,518 (n = 976)	>2,518–3,191.3 (n = 979)	>3,191.3–3,962.2 (n = 967)	>3,962.2 (n = 960)		
2-h glucose (mg/dL)	3.95 (-2.41, 10.32)	1.29 (-3.79, 6.36)	0.94 (-3.36, 5.23)	Ref.	.24	0.18 (-2.82, 3.17)
Fasting insulin (IU/mL)	0.93 (-0.03, 1.89)	0.66 (-0.11, 1.42)	0.48 (-.17, 1.12)	Ref.	.07	0.70 (0.26, 1.15)
Matsuda ISI	-0.61 (-0.94, -0.29)	-.42 (-0.68, -0.16)	-0.18 (-.39, 0.04)	Ref.	<.001	-0.29 (-0.44, -0.14)
Gutt index	-5.45 (-8.93, -1.97)	-3.52 (-6.29, -0.74)	-1.53 (-3.88, 0.82)	Ref.	.001	-2.20 (-3.84, -0.56)
Stumvoll β-cell function index (pmol/L)	105.7 (18.9, 192.6)	98.0 (28.6, 167.3)	38.2 (-20.4, 96.8)	Ref.	.007	83.9 (43.1, 124.6)

Notes: *Adjusted for age, race (black, nonblack), sex, clinic site, BMI, waist circumference, physical activity, smoking (never, former, current), alcoholic drinks per week (0, <7, 7+), systolic BP, ACE-I use, beta-blocker use, diuretic use, diet score, and total energy intake.

[†]Standard deviation of dietary potassium = 3,294 mg/d.

Table 4. Multivariate Models of the Association Between Serum and Dietary Potassium and Diabetes Risk Among CHS Participants Over 12 Years of Follow-Up

	Median	Cases of Incident Diabetes	Unadjusted Incidence Per 1,000 Person Years	Hazard Ratio (95% confidence interval)	
				Model 1*	Model 2 [†]
Serum potassium (mEq/L)					
≥4.5	4.7	71	8.6 (6.8, 10.9)	1.00 (ref)	1.00 (ref)
4.0-<4.5	4.2	253	8.2 (7.3, 9.3)	0.91 (0.70, 1.19)	0.89 (0.68, 1.16)
<4.0	3.7	121	9.1 (7.6, 10.9)	0.98 (0.72, 1.32)	0.87 (0.63, 1.19)
				<i>p</i> _{trend} = .99	<i>p</i> _{trend} = .43
Dietary potassium intake (mg/d)					
>3,962.2	4,519.4	83	7.22 (5.82, 8.95)	1.00 (ref)	1.00 (ref)
>3,191.3–3,962.2	3,555.1	100	8.66 (7.12, 10.53)	1.22 (0.91, 1.63)	1.19 (.85, 1.67)
>2,518–3,191.3	2,866.9	80	6.93 (5.57, 8.63)	.95 (0.70, 1.30)	0.83 (.55, 1.25)
≤2,518	2,111.4	112	9.80 (8.14, 11.79)	1.36 (1.02, 1.82)	1.13 (.68, 1.87)
				<i>p</i> _{trend} = .13	<i>p</i> _{trend} = .87

Notes: *Model 1: adjusted for age, sex, race, and clinic site.

[†]Model 2: adjusted for age, sex, race, clinic site, BMI, waist circumference, physical activity, smoking, alcohol use, systolic blood pressure, and use of ACE-I, beta blockers, and diuretics (also diet score and total energy intake for dietary analyses).

between low dietary potassium intake and increased risk of diabetes, with a HR (95% CI) of 1.36 (1.02, 1.82) for those with the lowest quartile of dietary potassium intake compared with the highest. However, after multivariate adjustment, this risk was attenuated and no longer statistically significant, with an adjusted HR (95% CI) of 1.13 (0.68, 1.87) for those in the lowest quartile of dietary potassium intake (Table 2). There were also no significant associations

between dietary potassium and risk of diabetes in the short term, at the end of 5 years of follow up. There were no statistically significant interactions between dietary potassium with age (*p* = .27), sex (*p* = .45), race (*p* = .68), or diuretic use (*p* = .65).

For analyses of both serum and dietary potassium, we found a similar pattern of associations among participants who were not on any diuretics.

DISCUSSION

In cross-sectional analyses of this cohort of older American adults, we did find a significant association between lower dietary potassium with reduced insulin sensitivity, along with compensatory increases in insulin secretion. We also found a similar trend with lower serum potassium and reduced insulin sensitivity and significantly increased insulin secretion. However, in the longitudinal assessment, we observed no significant associations of serum potassium concentration or dietary potassium intake with long-term diabetes risk. As in earlier studies, our results suggest that certain risk factors for diabetes observed in younger populations, but not all, may not markedly affect risk of diabetes among adults who remain free of diabetes into older age (26–28). We can hypothesize that older adults who have been without diabetes may be at less risk for developing frank diabetes due to conditions associated with aging such as loss of muscle mass and changes in insulin sensitivity that vary by target organ. However, further study is needed to determine this definitively.

Studies utilizing *in vitro* techniques or experimentally induced hypokalemia on healthy volunteers have tried to determine the biological mechanism of the association between thiazide-induced hypokalemia and impaired glucose tolerance with conflicting results. Some older studies found that hypokalemia was associated with increased insulin resistance by peripheral tissues (9,10). Other studies found that low potassium led to decreased insulin secretion (11–13). A more recent study involving obese participants found that a low-potassium catabolic diet led to both decreased insulin secretion and increased insulin resistance at postinsulin receptor sites, as measured by euglycemic clamps and evaluation of monocyte insulin receptors. Both of these defects in glucose metabolism were found to be reversed with potassium supplementation (29). Therefore, the precise mechanism by which low potassium may affect insulin secretion and insulin sensitivity is not clear.

Two recent cross-sectional analyses have found low-potassium, serum and dietary, to be associated with (a) prediabetes, but only among participants with hypertension and (b) metabolic syndrome, both conditions associated with increased insulin resistance (30,31). Our analyses of the CHS cohort, utilizing 2-hour OGTT data, also suggest that low-normal potassium contributes to the development of abnormal glucose metabolism predominantly by increasing insulin resistance. However, in this population, the β -cell response to insulin resistance appeared to be largely intact, with appropriately increased insulin secretion.

Compared with younger adults, older adults without a diagnosis of diabetes have both reduced insulin sensitivity as well as reduced beta-cell function (32). Abnormal glucose metabolism without diabetes, particularly insulin resistance, does have health consequences. High insulin levels and insulin resistance are associated with hypertension and cardiovascular disease (33). In older adults, insulin resistance has been associated with the development of

frailty (32,34). Determining risk factors for the development of insulin resistance could lead to the development of interventions to reduce insulin resistance and prevent development of these associated conditions.

Strengths of this study include the availability of measured potassium and glucose levels, a 2-hour OGTT, extensive data on potential confounders, a large sample size that increased precision and permitted simultaneous statistical adjustment for multiple variables, and long duration of follow-up that offered the opportunity to study long-term risk.

At the same time, these analyses have specific limitations. We did not have gold standard measures of insulin resistance and β -cell function such as euglycemic and hyperglycemic clamp studies. However, the formulae that we used to calculate insulin sensitivity and β -cell function have been validated with clamp data (17,18). Also, for these analyses, we used only two time points for measures of serum potassium and only baseline data for dietary potassium intake. Both of these measures are likely to vary over time, as evidenced by the low intraclass correlation coefficient of serum K over different visits, potentially reducing our ability to identify true associations.

In conclusion, although we did not identify serum and dietary potassium as risk factors for incident diabetes in older adults, results from cross-sectional analyses suggest that both of these novel risk factors, but particularly lower dietary potassium, are associated with increased insulin resistance. This relationship with insulin resistance needs to be confirmed, and its importance on diabetes risk, cardiovascular risk, and conditions specific to older adults should be determined as well.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest associated with this manuscript.

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