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Original Contribution

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Arjun Seth, BS; Yasmin Mossavar-Rahmani, PhD; Victor Kamensky, MS; Brian Silver, MD; Kamakshi Lakshminarayan, MD; Ross Prentice, PhD; Linda Van Horn, PhD; Sylvia Wassertheil-Smoller, PhD

Background and Purpose—Dietary potassium has been associated with lower risk of stroke, but there are little data on dietary potassium effects on different stroke subtypes or in older women with hypertension and nonhypertension.

Methods—The study population consisted of 90 137 postmenopausal women aged 50 to 79 at enrollment, free of stroke history at baseline, followed up prospectively for an average of 11 years. Outcome variables were total, ischemic, and hemorrhagic stroke, and all-cause mortality. Incidence was compared across quartiles of dietary potassium intake, and hazard ratios were obtained from Cox proportional hazards models after adjusting for potential confounding variables, and in women with hypertension and nonhypertension separately.

Results—Mean dietary potassium intake was 2611 mg/d. Highest quartile of potassium intake was associated with lower incidence of ischemic and hemorrhagic stroke and total mortality. Multivariate analyses comparing highest to lowest quartile of potassium intake indicated a hazard ratio of 0.90 (95% confidence interval, 0.85–0.95) for all-cause mortality, 0.88 (95% confidence interval, 0.79–0.98) for all stroke, and 0.84 (95% confidence interval, 0.74–0.96) for ischemic stroke. The effect on ischemic stroke was more apparent in women with nonhypertension among whom there was a 27% lower risk with hazard ratio of 0.73 (95% confidence interval, 0.60–0.88), interaction $P<0.10$. There was no association with hemorrhagic stroke.

Conclusions—High potassium intake is associated with a lower risk of all stroke and ischemic stroke, as well as all-cause mortality in older women, particularly those who are not hypertensive. **(*Stroke*. 2014;45:00-00.)**

Key Words: hypertension ■ postmenopause ■ potassium, dietary ■ stroke

Stroke is the fourth leading cause of mortality in the United States, and women account for 60% of all US stroke cases.[1] Women also have a higher lifetime risk of stroke than men.[2] There is interest in studying lifestyle factors, such as diets rich in potassium, that may reduce stroke risk.

Evidence from prospective studies suggests that higher dietary potassium intake is associated with reduced risk of stroke.[3–5] Three studies have specifically reported the effects of dietary potassium on risk of stroke in women. Khaw and Barret-Connor[3] found that women consuming <49 mmol (1911 mg) of potassium had a relative risk of 4.8 (P=0.01) when compared with women eating >49 mmol of potassium. Iso et al[6] found that women in the highest quintile of potassium intake (median, 3555 mg) versus the lowest quintile (median, 2017 mg) had a relative risk of 0.72 (95% confidence interval [CI], 0.51–1.01). Larsson et al[7] in the Swedish Mammography Cohort found that women with a history of hypertension had a relative risk of 0.64 (0.45–0.92) for all stroke types when comparing highest quintile of potassium intake with lowest quintile (mean, 3845 versus 2363 mg). In contrast, The European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) study[8] found that potassium intake was not associated with stroke. Despite these useful contributions, it remains unclear whether higher dietary potassium intake is associated with reduced risk of all subtypes of stroke and whether these findings are especially relevant in specific population subgroups.

The Women's Health Initiative Observational Study (WHI-OS), the largest prospective cohort study of postmenopausal women with long-term follow-up, was used to assess whether higher dietary potassium consumption is associated with reduced risk of total, ischemic or hemorrhagic stroke, and all-cause mortality. We also evaluated effects on ischemic stroke subtypes as determined by the Trial of ORG 10172

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From the Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY (A.S., Y.M.-R., V.K., S.W.-S.); Department of Neurology, Rhode Island Hospital/Warren Alpert Medical School of Brown University, Providence (B.S.); Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis (K.L.); Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA (R.P.); and Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL (L.V.H.).

Correspondence to Sylvia Wassertheil-Smoller, PhD, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, 1300 Morris Park Ave, Belfer Building, Rm 1312, Bronx, NY 10461. E-mail Sylvia.smoller@einstein.yu.edu

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Acute Stroke Trial (TOAST) classification, which previous studies have not investigated.

Subjects and Methods

Study Population

A detailed description of the WHI-OS is published.[9] Briefly, between 1993 and 1998, 93 676 women aged 50 to 79 years were recruited from 40 states and followed up prospectively for a mean of 11.1 years (range, 0.14–16.0 years). We excluded women with history of stroke at baseline (n=1354), those with missing information on history of stroke (n=54), and those with no information on dietary potassium (n=96). Finally, we also excluded as outliers n=2035 women in the bottom 1% of caloric intake (<465 calories), whose potassium intake ranged from 0.07 to 1790 mg, and women in the top 1% of caloric intake (>3931 calories), whose potassium intakes ranged from 1507 to 31 129 mg. Therefore, we had an analytic cohort of 90 137.

Dietary Assessment of Potassium

Participants completed food frequency questionnaires (FFQ) at enrollment and year 3 of follow-up. Details about diet assessment and the FFQs have been described elsewhere.[9,10] Briefly, participants completed questionnaires that reflected their dietary habits for the 3 months before enrollment. The questionnaire consisted of 3 sections: adjustment questions, food line items, and summary questions. The 19 adjustment questions allowed for more detailed analysis of fat intake by asking participants how foods were prepared. The list of 122 food line items specified type and frequency of various foods and food group intake according to small, medium, or large portion sizes. The 4 summary questions asked about intake of fruits, vegetables, and fat added to foods or in cooking. The FFQ nutrient database was derived from the University of Minnesota Nutrition Coordinating Center Nutrient Data for Scientific Research (NDSR) database for women in our analytic cohort.

Measurement properties of the WHI FFQ were evaluated in a subcohort of WHI and found to be similar to other dietary assessments used in the WHI, such as dietary recalls.[10] The Pearson correlation coefficient between the FFQ and 8 days of dietary intake from combined 4 days of dietary recalls plus 4 days of food records was 0.58 for dietary potassium.[10] In our own analysis, the correlation between intake at baseline and intake at year 3 in the WHI observational study was 0.63, indicating that potassium intake is fairly stable.

Ascertainment of Health Outcome

Ascertainment of death was determined based on the death certificate, medical records, or other records, such as autopsy report.[11] Mortality cause was initially adjudicated by a local physician adjudicator at the Clinical Centers for the WHI and then centrally adjudicated by 2 physicians. The 2 central adjudicators were required to review all deaths and come to agreement before closing the case.

Stroke was initially identified through self-report at annual visits, and medical records were then requested. Stroke was defined as rapid onset of neurological deficit lasting >24 hours and without evidence of other causes. Outcomes were adjudicated by a local physician adjudicator who then assigned a diagnosis based on medical records and WHI criteria, which have been defined elsewhere.[12,13] More than 95% of WHI stroke classification was based on MRI or computed tomographic findings.[13] Neurologists then centrally adjudicated locally determined strokes. A comparison of adjudicated strokes in the WHI versus stroke events defined in Medicare data showed substantial agreement between the 2 for all stroke (κ=0.69),[14] suggesting that WHI stroke ascertainment is a valid measure of stroke outcome.

Stroke was classified as ischemic stroke if diagnosis revealed an occlusion of cerebral or precerebral arteries with infarction (cerebral thrombosis, cerebral embolism, or lacunar infarction).[12,13] Central adjudicators then further classified ischemic stroke according to the TOAST classification. The TOAST classification is based on presumed underlying stroke cause and requires detailed investigation through brain imaging and methods described elsewhere.[12,15] Stroke was classified as hemorrhagic if diagnosis revealed a subarachnoid hemorrhage, intracerebral hemorrhage, or other intracranial hemorrhage not resulting from a procedure.[12,16]

Measurements of Covariates

Participants completed demographic and lifestyle questionnaires and physical measurements during baseline visits to a WHI Clinical Center. Demographic factors included date of birth and ethnicity (categories consistent with the 1990 US Census). Body mass index was calculated by dividing weight in kilograms by the square of the height in meters. Past smokers were those who self-reported having smoked ≥100 cigarettes and were currently not smoking. Alcohol intake was defined as number of drinks in a given time. Women were classified as hypertensive if they were either taking antihypertensive medications or had a systolic blood pressure ≥140, or a diastolic blood pressure ≥90. Participants who had ever taken any aspirin-containing medications were classified as aspirin users. Participants who took hormone therapy for >3 months but were not currently using hormone therapy were classified as past hormone therapy users. Hormone therapy was based on estrogen and progesterone pill and patches only; creams and shots were excluded. Self-report of doctor diagnosis was used for diabetes mellitus (sugar-related diabetes mellitus when not pregnant), for history of myocardial infarction, and for having high cholesterol requiring pills. Recreational physical activity was assessed using information about frequency, duration, and intensity of activity and organized into categories of activity as described elsewhere.[9]

Statistical Methods/Analysis

Quartiles of dietary potassium were obtained. We examined the mean and 95% CIs of dietary potassium by demographic variables and by covariates that have been reported to increase the risk of stroke. All probability values for any differences across the various categories of each covariate were obtained by ANOVA or χ^2. We also calculated the incidence of stroke and death per thousand person-years across quartiles of potassium intake and did linear trend analyses.

Hazard ratios (HRs) were estimated from Cox proportional hazards models comparing highest quartile with lowest quartile of potassium intake. We also considered an analysis of potassium per kilocalorie (K/kcal) using quartile cut points of K/kcal. However, because absolute potassium is more stably assessed with FFQ than are calories, an estimate of effect of nutrient density on stroke would not be as reliable. The correlation between potassium assessed by FFQ and 8 days of dietary records is 0.58, whereas the corresponding correlation for calories is 0.37.[10] Because potassium intake may be related to blood pressure, and because hypertension may be in the pathway between potassium intake and stroke, and also because hypertension is a major risk factor for stroke, we considered hypertensive status a priori for stratified analyses. Follow-up time was calculated in months from the date of enrollment to the date of first stroke, death, or end of the follow-up whichever came first. Model 1 is unadjusted; model 2 is adjusted for age, race, and hypertension status; and model 3 is adjusted for model 2 variables plus smoking, recreational physical activity, history of diabetes mellitus, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol requiring pills, and body mass index. We examined each of these variables separately for interaction with potassium intake by including an interaction term of the variable and potassium intake in model 3 for ischemic stroke. When the interaction terms were significant with $P<0.10$, we did stratified analyses for that variable. Statistical analyses were performed using SAS software (SAS Institute Inc, Cary, NC).

Results

The analytic cohort of 90 137 postmenopausal women with no history of stroke at baseline, had mean age 63.6 years at baseline, and had SD 7.4 years. Mean dietary potassium intake was 2611 mg/d. Blacks, current smokers, and nondrinkers of alcohol reported lower dietary potassium intakes (Table 1). Those

Table 1. Baseline Potassium Intake by Characteristics

	Dietary Potassium, mg		
	n	Mean (95% CI)	*P* Value*
Whole cohort	90 137	2611 (2605–2618)	...
Age, y			
50 to 59	28 675	2589 (2578–2600)	<0.001
60 to 69	39 739	2625 (2615–2634)	
70 to ≥79	21 723	2616 (2603–2629)	
Ethnicity			
White	75 842	2684 (2678–2691)	<0.001
Black	6848	2145 (2122–2168)	
Hispanic	3301	2274 (2240–2309)	
Other	3909	2304 (2274–2335)	
Education			
0–8 y or some high school	4353	2199 (2170–2228)	<0.001
High-school diploma: some college	47 004	2519 (2511–2528)	
College graduate or postgraduate	38 061	2772 (2763–2782)	
Income			
<$20 000	12 897	2428 (2411–2446)	<0.001
$20 000–$49 999	36 353	2609 (2599–2619)	
≥$50 000	34 334	2692 (2682–2702)	
Do not know	2608	2506 (2467–2545)	
Marital status			
Never	4232	2655 (2624–2685)	<0.001
Divorced or separated	13 991	2537 (2520–2553)	
Widowed	15 410	2560 (2544–2576)	
Presently married	54 619	2642 (2634–2650)	
Marriage-like relationship	1459	2591 (2542–2639)	
Smoking history			
Current	5441	2362 (2337–2387)	<0.001
Past	38 194	2646 (2637–2656)	
Never	45 239	2613 (2603–2622)	
Alcohol intake			
None/nondrinker	9809	2429 (2409–2449)	<0.001
Past drinker	16 455	2527 (2511–2542)	
<1 drink/mo	10 347	2537 (2519–2556)	
<1 drink/wk	18 105	2608 (2594–2622)	
1 to <7 drinks/wk	23 371	2709 (2697–2721)	
≥7 drinks/wk	11 474	2769 (2752–2785)	
Recreational physical activity			
No activity	11 904	2341 (2324–2358)	<0.001
Some activity of limited duration	34 071	2534 (2524–2545)	
2 to <4 episodes/wk	16 603	2679 (2665–2693)	
4 episodes/wk	26 559	2791 (2779–2802)	
Hormone use			
Current	43 123	2630 (2621–2639)	<0.001
Past	18 663	2604 (2590–2618)	
Never	26 732	2582 (2570–2594)	
Weight status, BMI, kg/m^2			
Underweight (<18.5)	1066	2550 (2491–2608)	0.039
Normal (18.5–24.9)	35 638	2616 (2606–2626)	
Overweight (25.0–29.9)	30 348	2606 (2596–2617)	
Obesity I (30.0–34.9)	13 859	2602 (2586–2619)	
Obesity II (35.0–39.9)	5120	2628 (2600–2656)	
Extreme obesity III (≥40.0)	3058	2610 (2574–2646)	
Systolic BP, mm Hg			
≤120	36 057	2633 (2623–2643)	<0.001
120–140	35 947	2607 (2597–2617)	
>140	18 011	2576 (2561–2590)	
Diastolic BP, mm Hg			
<90	84 347	2616 (2610–2623)	<0.001
≥90	5649	2538 (2512–2564)	
Hypertension (if self-reported treatment or BP ≥140/90, mm Hg)			
Yes	34 277	2573 (2563–2583)	<0.001
No	54 635	2637 (2629–2645)	
High cholesterol (requiring pills ever)			
Yes	12 991	2574 (2557–2590)	<0.001
No	75 171	2620 (2613–2627)	
Aspirin use (any)			
Yes	31 768	2679 (2668–2689)	<0.001
No	58 369	2575 (2567–2582)	
History of diabetes mellitus			
Yes	4855	2558 (2529–2587)	<0.001
No	85 205	2614 (2608–2621)	
History of MI			
Yes	2020	2534 (2490–2577)	<0.001
No	88 056	2613 (2607–2619)	
History of atrial fibrillation			
Yes	4089	2624 (2594–2655)	0.821
No	84 603	2613 (2606–2619)	
History of CABG/PTCA			
Yes	1602	2535 (2486–2583)	<0.001
No	87 121	2615 (2608–2621)	
History of CHD			
Yes	2871	2547 (2511–2584)	<0.001
No	85 863	2616 (2609–2622)	

(*Continued*)

BP indicates blood pressure; BMI, body mass index; CABG, coronary artery bypass graft; CHD, coronary heart disease; CI, confidence interval; MI, myocardial infarction; and PTCA, percutaneous transluminal coronary angioplasty.

*P values were obtained from χ^2 tests or ANOVA across the various categories of each covariate.

who reported ≥2 episodes of recreational physical activity a week had greater dietary potassium intake than those who reported limited or no activity.

Table 2. All-Cause Mortality and Stroke Rates by Quartiles of Dietary Potassium Intake

		All-Cause Mortality		Stroke (All)		Stroke (No Hx of MI)		Ischemic Stroke		Hemorrhagic Stroke	
Quartiles of Dietary Potassium, mg	Participant Number	Event Number	Annualized Rate*	Event Number	Annualized Rate*	Event Number	Annualized Rate*	Event Number	Annualized Rate*	Event Number	Annualized Rate*
Q1: <1925.5	22 534	3096	13.03	793	3.40	750	3.29	574	2.48	125	0.55
Q2: ≥1925.5–2519.4	22 534	2921	11.65	769	3.12	732	3.03	542	2.21	128	0.53
Q3: >2519.4–3193.6	22 535	2685	10.52	719	2.86	687	2.78	530	2.12	106	0.43
Q4: ≥3193.6	22 534	2894	11.30	765	3.03	734	2.96	544	2.17	125	0.51
Overall	90 137	11 596	11.60	3046	3.10	2903	3.01	2190	2.24	484	0.50

P for trend for all-cause mortality=0.0002, no significance for other end points. MI indicates myocardial infarction.
*Annualized rate is defined as number of events per 1000 person-years.

Stroke Incidence

Incidence per 1000 person-years was 3.10 for all stroke, 2.24 for ischemic stroke, 0.50 for hemorrhagic stroke, and 11.60 for all-cause mortality. Those in the lowest quartile of estimated dietary potassium intake (<1925.5 mg potassium) had higher estimated incidence than those in other quartiles across all outcomes (Table 2). There was a statistically significant linear trend for mortality (*P*=0.0002), but the linear trend test did not reach statistical significance for the other outcomes.

Dietary Potassium and Stroke Risk

Table 3 shows a statistically significant lower risk in all quartiles of potassium intake compared with lowest quartile, for all-cause mortality, all stroke, and ischemic stroke, in unadjusted, age-, race-, hypertension-adjusted, and multivariate-adjusted models (Table 3). In a sensitivity analysis excluding those with previous myocardial infarction, the HRs and CIs were similar to those for all stroke (data not shown). The HR in the fully adjusted model comparing highest quartile (Q4) with the lowest quartile (Q1) of potassium

Table 3. HRs for All-Cause Mortality and Stroke by Quartiles of Potassium

	Quartiles of Potassium, mg			
	Q1: <1925.5	Q2: 1925.5–2519.4; HR, 95% CI	Q3: >2519.4–3193.6; HR, 95% CI	Q4: >3193.6; HR, 95% CI
All-cause mortality				
Model (1)	1	0.87 (0.82–0.91)	0.77 (0.74–0.82)	0.83 (0.79–0.87)
Model (2)	1	0.87 (0.82–0.91)	0.78 (0.74–0.82)	0.83 (0.79–0.87)
Model (3)	1	0.91 (0.86–0.96)	0.84 (0.79–0.89)	0.90 (0.85–0.95)
Stroke (all)				
Model (1)	1	0.89 (0.81–0.99)	0.82 (0.74–0.91)	0.87 (0.79–0.96)
Model (2)	1	0.90 (0.81–1.00)	0.83 (0.75–0.92)	0.88 (0.79–0.97)
Model (3)	1	0.88 (0.79–0.98)	0.85 (0.76–0.94)	0.88 (0.79–0.98)
Ischemic stroke				
Model (1)	1	0.88 (0.78–0.99)	0.84 (0.74–0.94)	0.85 (0.76–0.96)
Model (2)	1	0.88 (0.78–0.99)	0.85 (0.75–0.95)	0.85 (0.76–0.96)
Model (3)	1	0.85 (0.75–0.96)	0.85 (0.75–0.97)	0.84 (0.74–0.96)
Hemorrhagic stroke				
Model (1)	1	0.95 (0.74–1.22)	0.77 (0.60–1.00)	0.91 (0.71–1.16)
Model (2)	1	0.96 (0.75–1.23)	0.75 (0.58–0.98)	0.90 (0.70–1.16)
Model (3)	1	0.91 (0.70–1.19)	0.78 (0.59–1.03)	0.92 (0.71–1.20)
TOAST subtype*				
Large artery atherosclerosis	1	0.95 (0.60–1.49)	0.85 (0.53–1.35)	0.69 (0.42–1.13)
Cardioembolism	1	0.91 (0.70–1.17)	1.01 (0.79–1.30)	1.04 (0.81–1.32)
Small-vessel occlusion (lacunae)	1	0.82 (0.62–1.08)	0.77 (0.59–1.03)	0.83 (0.63–1.10)

Model (1): unadjusted; model (2): adjusted for age, race, and hypertension status; model (3): adjusted for model 2 variables plus smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and body mass index. CI indicates confidence interval; HR, hazard ratio; and TOAST, Trial of ORG 10172 Acute Stroke Trial.
*All adjusted for all variables in model (3).

Table 4. HRs for All-Cause Mortality and Stroke in Quartiles of Potassium by Hypertension Status

	Quartiles of Potassium, mg			
	Q1: <1925.5	Q2: ≥1925.5–2519.4; HR, 95% CI	Q3: >2519.4–3193.6; HR, 95% CI	Q4: >3193.6; HR, 95% CI
All-cause mortality				
Hypertension	1	0.92 (0.85–0.99)	0.85 (0.79–0.92)	0.89 (0.82–0.96)
No hypertension	1	0.91 (0.84–0.98)	0.84 (0.77–0.91)	0.92 (0.85–1.00)
Stroke (all)				
Hypertension	1	0.99 (0.86–1.13)	0.93 (0.81–1.07)	0.97 (0.84–1.12)
No hypertension	1	0.75 (0.64–0.89)	0.75 (0.64–0.89)	0.79 (0.67–0.93)
Ischemic stroke				
Hypertension	1	0.96 (0.82–1.14)	0.96 (0.81- 1.13)	0.93 (0.79–1.10)
No hypertension	1	0.71 (0.58–0.86)	0.73 (0.60–0.88)	0.73 (0.60–0.88)
Hemorrhagic stroke				
Hypertension	1	0.81 (0.56–1.18)	0.85 (0.59–1.24)	0.85 (0.58–1.24)
No hypertension	1	1.02 (0.70–1.49)	0.72 (0.48–1.09)	1.01 (0.69–1.48)
TOAST subtype				
Large artery atherosclerosis				
Hypertension	1	1.13 (0.65–1.96)	0.92 (0.51–1.65)	0.66 (0.35–1.25)
No hypertension	1	0.67 (0.30–1.49)	0.74 (0.34–1.59)	0.72 (0.33–1.57)
Cardioembolism				
Hypertension	1	0.99 (0.71–1.38)	1.06 (0.76–1.48)	1.17 (0.85–1.61)
No hypertension	1	0.80 (0.54–1.19)	0.95 (0.65–1.38)	0.87 (0.60–1.28)
Small-vessel occlusion (lacune)				
Hypertension	1	1.11 (0.80–1.56)	0.90 (0.63–1.28)	0.95 (0.67–1.36)
No hypertension	1	0.43 (0.26–0.71)	0.60 (0.38–0.95)	0.67 (0.43–1.04)

Adjusted for age, race, hypertension status, smoking status, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and body mass index. CI indicates confidence interval; HR, hazard ratio; and TOAST, Trial of ORG 10172 Acute Stroke Trial.

intake was 0.90 (95% CI, 0.85–0.95) for all-cause mortality, 0.88 (95% CI, 0.79–0.98) for all stroke, and 0.84 (95% CI, 0.74–0.96) for ischemic stroke. There was no association with hemorrhagic stroke.

In accordance with our a priori analysis plan, we present results for all outcomes of interest stratified by hypertension status (Table 4). Among women with nonhypertension, there was a lower risk of all-cause mortality, all stroke, and ischemic stroke across increasing quartiles for potassium. In particular, there was a 27% lower risk of ischemic stroke when comparing Q4 to Q1 in model 3 (HR, 0.73; 95% CI, 0.60–0.88) and no association for hemorrhagic stroke. Among women with hypertension, higher potassium intake was associated with lower all-cause mortality, but there was no association with any stroke outcome.

Interactions were observed for ischemic stroke between dietary potassium and hypertension ($P<0.10$), diabetes mellitus ($P<0.05$), high cholesterol requiring pills ($P<0.01$), and body mass index ($P<0.05$). The Figure shows stratified analyses by these variables. For example, among the 35 227 women who had normal body mass index, there were 727 ischemic stroke events. The HR comparing the highest quartile with the lowest quartile of potassium intake indicates that among those of normal weight, higher potassium intake was associated with a 30% lower risk of stroke (HR, 0.70; 95% CI, 0.56–0.87).

Subtypes of Ischemic Stroke According to TOAST Classification

Cox proportional hazards models were run for the predominant TOAST classes: large artery atherosclerosis, cardioembolism, and small-vessel occlusion (lacunae). We compared each subtype with a reference group of no stroke. Power to detect effects was small for these subgroups. Nevertheless, higher potassium intake was associated with a lower risk of small-vessel disease among those not hypertensive. When compared with the lowest quartile, Q2, Q3, and Q4 had HRs (95% CI) of 0.43 (0.26–0.71), 0.60 (0.38–0.95), and 0.67 (0.43–1.04), respectively.

Discussion

In the largest US cohort study of ≥90 000 postmenopausal women, we found an inverse association between self-reported dietary potassium intake and incidence of ischemic stroke. The lower risk of stroke associated with higher intake of potassium persisted after adjusting for multiple covariates. In particular, women consuming the highest quantity of potassium in our cohort (>3193.6 mg) had a 12% lower risk of all-type stroke (HR, 0.88; 95% CI, 0.79–0.98) and a 16% lower risk of ischemic stroke (HR, 0.84; 95% CI, 0.74–0.96) when compared with women consuming <1925.5 mg of potassium.

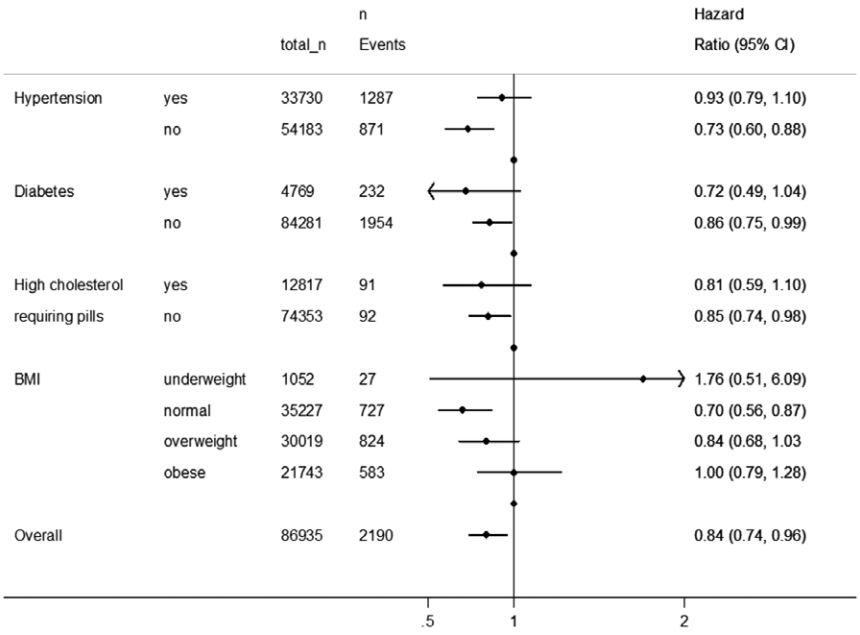

Figure. Hazard ratios comparing highest to lowest quartile of potassium intake (milligram) for ischemic stroke stratified by hypertension, diabetes mellitus, high cholesterol, and body mass index (BMI). Hazard ratios adjusted for age, race, hypertension, smoking, physical activity, history of diabetes mellitus, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and BMI. Variables that make up the strata are omitted when running Cox regressions in that stratum. CI indicates confidence interval.

Women with nonhypertension tended to benefit the most from consuming diets higher in potassium. Women in the highest quartile of potassium intake had a 21% reduction in risk of all-type stroke (HR, 0.79; 95% CI, 0.67–0.93) and a 27% reduction in risk of ischemic stroke (HR, 0.73; 95% CI, 0.60–0.88). Women with hypertension had a lower total mortality risk with higher potassium intake but no lowered risk of stroke, suggesting that higher potassium intake may be of more benefit before hypertension develops. This finding supports cell culture and animal model studies that have shown that higher potassium levels improve vascular endothelial function and promote nitric oxide release, thereby improving vascular flow[17,18] In women with nonhypertension, the correlation between systolic blood pressure and potassium intake was negligible at −0.008, suggesting that in our data, the beneficial effect of potassium intake among nonhypertensives was not modulated by its effect on blood pressure. Instead, this particular result may be because of habitually higher intakes of dietary potassium that prevent arterial stiffness.[19] A small study of young men and women found that habitually low potassium intake was associated with increased arterial stiffness, measured by carotid-femoral pulse wave velocity, despite normal blood pressures. This suggests that dietary potassium may have an effect on blood vessels beyond its effects on blood pressure.[19] Additional research to elucidate mechanisms is needed.

The US Department of Agriculture currently recommends that women eat ≥4700 mg of potassium daily.[20] In WHI, only 2.8% of women met or exceeded this level. The World Health Organization recently amended its recommendation after conducting a meta-analysis of dietary potassium intake and cardiovascular disease and advises that women eat ≥3510 mg of potassium[21] per day.[22] In the WHI-OS cohort, 16.6% of women met or exceeded this level. Overall, the mean reported dietary potassium intake was only 2611 mg. Few postmenopausal women seem to reach the recommended levels of daily potassium intake.

Furthermore, the National Health and Nutrition Examination Survey comparing the period from the 1988 to 1994 with the 2003 to 2008 survey reports that mean dietary potassium intake declined among women aged 51 to 70 years by 87 to 2419 mg and in those >71 years by 173 to 2234 mg.[23] This decline is predicted to continue unless major changes in the food environment provide more unprocessed meats, fruits, and vegetables to consumers. Some foods rich in potassium are white and sweet potatoes, bananas, and white beans. Our results illustrate that consuming more potassium, even below recommended levels, is associated with a reduced risk of all-type stroke and ischemic stroke by ≥20% in women with nonhypertension. With the general decline in potassium consumption, women may be at greater risk of having strokes. Healthcare providers, therefore, may wish to reinforce the importance of a potassium-rich diet especially among postmenopausal women.

The difference between our results and those from the Swedish Mammography Cohort (SMC) and EPIC cohort studies can be explained in several ways. Our study was substantially larger than the SMC, and our measurement of hypertension was more robust than SMC, which relied on self-reported history of hypertension without subsequent validation.[7] This influenced their finding that an increase in potassium intake is more protective for women with hypertension. Our study looked exclusively at older women, unlike the EPIC-NL study which looked at a group of 36 094 men and women with a mean age of 49 years.[8] The mean dietary potassium intake was also substantially lower in women from the WHI than in the EPIC-NL study participants (2611 versus 3672 mg). The generally higher potassium intakes in their analysis may have prevented them from finding an association with stroke.

There are some limitations to our study. First, this was an observational study rather than a clinical trial and, therefore, results must be interpreted with caution on causation. Second, our estimates of potassium intake come from FFQ and may under- or overestimate true intake. Third, we only used baseline dietary potassium in assessing relationships with outcomes. WHI-OS participants also completed FFQs at year 3 of follow up. Comparing the dietary potassium intake

between baseline and year 3, there was a mean decrease in potassium intake of 79 mg, with a correlation of 0.63 between baseline and year 3. Fourth, our analyses focus on potassium only, whereas corresponding sodium consumption may be an important covariate in determining hypertension[24] and cardiovascular disease[21] risk. However, sodium consumption is not reliably estimated by the WHI FFQ, so analyses of potassium and sodium jointly in relation to these outcomes in the WHI-OS need to rely on biomarkers for sodium consumption,[25] which are not available on the entire cohort.

In summary, in the largest prospective study of older women with long-term follow-up, we found lower risk of ischemic but not hemorrhagic stroke associated with higher intakes of potassium, especially in women with nonhypertension, as well as lowered risk of all-cause mortality in all women. We also found that higher potassium intake is associated with lower risk of small-vessel stroke subtype. Because dietary intake of potassium in the United States is well below the recommended intake, these findings are important in suggesting preventive dietary measures to lower the risk of stroke.

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Disclosures

None.

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