Dietary Potassium Intake and Stroke Mortality

Jing Fang, MD; Shantha Madhavan, DrPH; Michael H. Alderman, MD

Background and Purpose—An inverse relationship of dietary potassium to stroke mortality in a small community has been previously reported. To further assess this association in a larger sample, we examined data from the first National Health and Nutrition Examination Survey (NHANES I) Epidemiological Follow-up Study.

Methods—We analyzed baseline data during 1971–1975 and follow-up through 1992. Dietary potassium intake, determined by 24-hour dietary recall at baseline, was available for 9866 subjects. Stroke mortality was recorded through 1992 follow-up.

Results—Mean age and dietary potassium at baseline were 55 years and 2084 mg/d; blacks reported significantly lower potassium intake than whites (1606 versus 2178 mg/24 h). During an average of 16.7 years of follow-up, there were 304 stroke deaths. For men, stratified by tertile of dietary potassium intake, age-adjusted stroke mortality rates per 1000 person-years for the lowest dietary potassium group were significantly higher than for the highest intake group, for both whites (1.94 versus 1.17; relative risk, 1.66; 95% CI, 1.32 to 2.14) and blacks (5.08 versus 1.19; relative risk, 4.27; 95% CI, 1.88 to 9.19). For women, there was no significant difference in stroke mortality between similar levels of potassium intake for either whites (1.61 versus 1.42; relative risk, 1.13; 95% CI, 0.84 to 1.66) or blacks (2.46 versus 3.04; relative risk, 0.80; 95% CI, 0.21 to 2.01). After stratification by hypertensive status, stroke mortality rates were significantly different by tertile of dietary potassium only for hypertensive men. There was no stroke mortality difference by potassium intake among hypertensive women or nonhypertensive men and women. Multivariate analysis, in which we controlled for caloric intake and other baseline cardiovascular risk factors, revealed that only among black men and hypertensive men was lower dietary potassium intake a predictor of stroke mortality.

Conclusions—The previous finding of an association of increasing dietary potassium intake with decreasing stroke mortality has been detected only among black men and hypertensive men in this study. (Stroke. 2000;31:1532-1537.)

Key Words: diet ■ mortality ■ observational study ■ potassium ■ stroke

Human observation and animal experimentation have suggested that increased potassium intake may protect against stroke.1–3 Epidemiological studies have reported a negative association of dietary potassium intake and stroke mortality.2,3 One study, based on a single 24-hour recall of dietary potassium intake, included 859 residents of a single homogeneous white community, among whom, over 12 years, there were 24 stroke-associated deaths.2 A more recent study, limited to men, employed a semiquantitative food frequency questionnaire to estimate potassium intake.3

To further explore the association of dietary potassium intake with stroke mortality in a more general population, we examined the experience of participants in the first National Health and Nutrition Examination Survey (NHANES I). Among this population of 9866, we have related baseline potassium intake measured by standardized quantitative methods in 1971–1975 to stroke mortality through 1992.

Subjects and Methods

Subjects
The NHANES I survey examined 20 729 individuals aged 25 to 74 years during 1971–1975. Of these, 14 407 (70%) underwent medical examination, and 11 348 had a nutritional assessment based on a 24-hour dietary recall. Data on potassium intake were missing for 1 subject, who was therefore excluded. Vital status for the remaining 11 347 participants was examined through 1992. This was determined by interview, tracing, and searches of the National Death Index. Deaths and causes of death were confirmed from death certificates. Details of the plan and operation of the NHANES I baseline survey4,5 and the NHANES I Epidemiological Follow-up4,6 have been previously published.

Of 11 347 subjects, 423 with unknown vital status were excluded. An additional 121 were excluded by virtue of not being either black or white. Of the remaining 10 803 subjects, the range of 24-hour dietary potassium was 1.02 to 11 358.07 mg/d. To minimize the instability of values, the extreme 1% in both tails was excluded, leaving 10 590 study subjects with dietary potassium ranging from 365.9 to 5699.4 mg/d. Further exclusion of those with a history of myocardial infarction and/or stroke (724) left 9866 as the subjects of this analysis.
Baseline Measurement
Data on nutrient intake were available from a single 24-hour dietary recall. Potassium intake was expressed as milligrams per day and total caloric intake as calories per day.

Other baseline information included medical history, standardized medical examination, laboratory tests, and anthropometric measures. A single blood pressure measurement was obtained by a physician at the beginning of the physical examination with a standard sphygmomanometer in accordance with American Health Association criteria. The baseline medical history questionnaire recorded selected medical conditions (eg, diabetes, heart disease) diagnosed by a physician. Body mass index (kg/m²) was computed from weight and height. The measurement of alcohol consumption was considered positive when the subjects consumed ≥2 drinks per week. Smoking status at baseline was only available for <50% of study subjects. For the rest, smoking status was derived from a questionnaire included in the 1982–1984 follow-up interview on lifetime smoking history. The validity of this approach has been documented. 8,9 The smoking status information used in this analysis is from the combination of the 2 sources of interview, so that smoking information was available for approximately 84% of participants.

Outcome Measures
Outcome information, based on interviews, healthcare facility medical records, and death certificates, was obtained in 4 waves of follow-up: 1982–1984, 1986, 1987, and 1992. Since information on mortality was cut off at June 30, 1992, for 1992 follow-up, participants not reported as dead before this date were presumed to be alive. Death was ascertained by either death certificate or a proxy respondent. The underlying cause of death was coded according to the International Classification of Diseases, Ninth Revision (ICD-9).

Stroke deaths were determined by ICD-9 codes 430 to 438. Through the 1992 follow-up, there were 3323 reported deaths (33.7%). Of these, 304 (9.1%) were due to stroke.

Statistical Analysis
The analysis was performed on 9866 study subjects. The analytical strategies were developed to examine the cross-sectional association of dietary potassium and other cardiovascular risk factors at baseline, as well as the association of dietary potassium with stroke mortality during follow-up.

The population was stratified into 3 groups by tertile of dietary potassium intake. Baseline characteristics of the 3 groups were defined. All statistical tests for continuous (Student’s t test) and categorical variables (χ² test) were 2-tailed. Since distributions of dietary potassium intake for men and women and for both races differed significantly, baseline characteristics were assessed according to sex/race-specific tertile of 24-hour dietary potassium intake, if possible. Sex-specific stroke mortality rate (per 1000 person-years), adjusted for age, was calculated by dietary potassium tertile, standardized by the direct method, with the total study population as reference. With the lowest tertile used as reference, the differences in mortality rates between the lowest and the other tertiles were tested for statistical significance with the Mantel-Haenszel test statistic. Furthermore, sex/race-specific age-adjusted stroke mortality rates were computed.

Because of the importance of hypertension as a risk factor for stroke, the analysis was done by stratifying subjects on the basis of those with and without hypertension. Hypertension status was self-reported by the subjects, ie, they reported that they had hypertension or were taking antihypertensive medication. For each sex, age/race-adjusted stroke mortality rates by tertile of dietary potassium intake were estimated for hypertensive and nonhypertensive subjects. With the lowest tertile as reference, the differences in mortality rates between the lowest and the middle as well as the highest tertile of dietary potassium were determined by the Mantel-Haenszel test statistic.

A Cox proportional hazards regression model was constructed among selected groups that differed significantly in stroke mortality rate by tertile of dietary potassium intake. In these models, dietary potassium intake by tertile, created as a dummy variable, entered the models as independent variable, and stroke mortality entered the models as dependent variable, adjusted for caloric intake (continuous variable) and controlling for other characteristics associated with stroke mortality such as age (continuous variable), smoking status (yes=1), cholesterol (continuous variable), and history of diabetes (yes=1). For hypertensive subjects, diuretic therapy was also included in the model.

Results
Baseline Characteristics
The 9866 study subjects were predominantly female (61.8%), white (83.5%), and younger than 55 years (59.7%) at baseline examination. Dietary potassium and caloric intake (mean±SD) were 2084.2±982.6 mg/d and 1740.7±797.6 kcal/d, respectively. Men had higher dietary potassium intake than did women (2444.3 versus 1862.1 mg/d; P<0.001), and whites had significantly higher intake than blacks (2178.3 versus 1606.6 mg/d; P<0.001). Mean dietary potassium and caloric intakes by sex and race are presented in Table 1. Blacks, both men and women, had significantly (P<0.001) lower dietary potassium, with calorie as well as potassium intake adjusted for calories (potassium/1000 kcal) compared with whites. Of note is that women, both blacks and whites, had lower potassium and caloric intake than men. Calorie-adjusted potassium was higher among women than among men.

At baseline, dietary potassium intake was positively related to dietary caloric intake for all sex and race groups (Table 2). In general, those with higher dietary potassium intake were younger and had sharply lower blood pressures than did those with lower dietary potassium intakes. The systolic blood pressure difference was more impressive than the diastolic. Serum cholesterol was not related to dietary potassium intake except among white women, in which case the relationship was negative. A relationship of dietary potassium to smoking existed only in white women, while diuretic use was inversely associated with dietary potassium intake only among white men. A history of diabetes was not associated with dietary potassium intake in all sex/race groups. Dietary potassium intake was positively associated with dietary caloric intake as well as potassium/1000 kcal.

Mortality
During 16.7 years of follow-up, there were 304 stroke deaths. Stroke mortality rates were significantly higher among blacks than whites (2.94 versus 1.64 per 1000 person-years; P<0.05) and among hypertensive subjects than nonhypertensive subjects (4.13 versus 1.21; P<0.05). Age/sex-adjusted
stroke mortality per 1000 person-years for blacks were 2.03 and 4.91 among nonhypertensives and hypertensives, respectively ($P < 0.05$), and among whites, the corresponding rates were 1.14 and 3.89, respectively ($P < 0.05$).

The dietary potassium and caloric intakes for men who died of stroke were significantly lower than for those who did not (Table 3). However, there were no significant differences in dietary potassium intake between women who died of stroke and those who did not. Finally, white women who succumbed to stroke consumed significantly fewer calories than those who did not. Of note, those who died of stroke were significantly older than those who did not in all subgroups.

Overall, sex-specific, age-adjusted stroke mortality by tertile of dietary potassium revealed that among men, the rates (1/1000 person-years) from the lowest to highest tertile were 2.57, 2.07, and 1.39, respectively ($P = 0.046$ for I versus II, and $P = 0.007$ for I versus III). Among women, the corresponding rates were 1.91, 1.87, and 1.81, with no statistical significance between the groups.

The subjects were stratified by sex and race into 4 groups (Table 4). Men in the lowest tertile of dietary potassium intake, both black and white, had significantly higher stroke mortality than did those with the highest intake. With the highest tertile as reference, the relative risk (RR) for blacks in the lowest tertile (RR, 4.27; 95% CI, 1.88 to 9.19) was more than double than that for whites (RR, 1.66; 95% CI, 1.32 to 2.14). Among women, regardless of race, there was no significant difference in stroke mortality by tertile of dietary potassium intake.

Stratification by hypertensive status revealed that among nonhypertensive subjects ($n = 7632$), after age/race adjustment, the sex-specific stroke mortality by dietary potassium intake was not significantly different between dietary potas-
sium intake groups for either men or women (Table 5). Among hypertensive subjects (n=2234), increased risk of stroke death was associated with low dietary potassium intake only among men; those with the lowest potassium intake had 2.13 times higher stroke mortality rate than did those in the highest potassium intake tertile.

We further performed Cox proportional hazard regression analysis among white men (n=3169) and black men (n=595), as well as hypertensive men (n=735). In these models, stroke mortality was the dependent variable, and dietary potassium by tertile was an independent variable, adjusted for dietary caloric intake. Other factors—age, smoking status, history of diabetes, and serum cholesterol level—were also controlled in these models, as well as diuretic use among hypertensive subjects (Figure). Among white men, after we controlled for caloric intake and other variables, dietary potassium intake was not a predictor for stroke mortality. However, among black men and hypertensive men, the association of a lower dietary potassium intake with higher stroke mortality persisted. For black men, those with the lowest potassium intake (1260 mg/d), compared with those with the highest potassium intake (2206 mg), had a 167% higher stroke mortality. For hypertensive men, those with the lowest potassium intake (1739 mg/d) had an 88%

TABLE 3. Mean Age, Dietary Potassium, and Caloric Intake by Stroke Mortality Status, by Sex and Race, NHANES I (1971–1975) and 1992 Follow-up

<table>
<thead>
<tr>
<th>Race</th>
<th>Stroke Death No.</th>
<th>Age</th>
<th>Potassium</th>
<th>Calorie</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>9562</td>
<td>48.8±15.6</td>
<td>2090.8±983.4</td>
<td>1748.9±800.6</td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>304</td>
<td>65.1±9.1</td>
<td>1878.5±306.3</td>
<td>1481.0±648.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>3076</td>
<td>51.5±15.3</td>
<td>2564.7±1036.2</td>
<td>2216.8±869.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt;0.001</td>
<td>P=0.016</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>93</td>
<td>65.4±8.1</td>
<td>2301.8±991.8</td>
<td>1831.6±641.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt;0.001</td>
<td>P=0.018</td>
<td>P=0.008</td>
</tr>
<tr>
<td>Black</td>
<td>567</td>
<td>53.6±15.3</td>
<td>1865.4±994.2</td>
<td>1949.1±875.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P&lt;0.001</td>
<td>P=0.018</td>
<td>P=0.008</td>
</tr>
</tbody>
</table>

Values are mean±SD unless indicated otherwise.

TABLE 4. Age-Adjusted Stroke Mortality by Tertile of Dietary Potassium, by Sex and Race, NHANES I (1971–1975) and 1992 Follow-up

<table>
<thead>
<tr>
<th>Whiters</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n=3764)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1.94 (37)</td>
</tr>
<tr>
<td>II</td>
<td>2.28 (39)</td>
</tr>
<tr>
<td>III</td>
<td>1.17 (17)</td>
</tr>
<tr>
<td>P</td>
<td>0.042</td>
</tr>
<tr>
<td>RR, 95% CI*</td>
<td>1.66, 1.32–2.14</td>
</tr>
<tr>
<td>Women (n=6102)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1.61 (50)</td>
</tr>
<tr>
<td>II</td>
<td>1.52 (49)</td>
</tr>
<tr>
<td>III</td>
<td>1.43 (37)</td>
</tr>
<tr>
<td>P</td>
<td>0.53</td>
</tr>
<tr>
<td>RR, 95% CI*</td>
<td>1.13, 0.84–1.66</td>
</tr>
</tbody>
</table>

Values in parentheses in body of table indicate deaths. Rates are per 1000 person-years.

*P value and RR (95% CI) for III vs I were calculated using the Mantel-Haenszel test statistic.

TABLE 5. Age/Race-Adjusted Stroke Mortality by Tertile of Dietary Potassium by Sex and Hypertension Status, NHANES I (1971–1975) and 1992 Follow-up

<table>
<thead>
<tr>
<th>Hypertensive subjects (n=2234)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6.02 (19)</td>
<td>4.43 (36)</td>
</tr>
<tr>
<td>II</td>
<td>4.63 (17)</td>
<td>3.34 (30)</td>
</tr>
<tr>
<td>III</td>
<td>2.82 (9)</td>
<td>3.80 (27)</td>
</tr>
<tr>
<td>P</td>
<td>0.0242</td>
<td>0.746</td>
</tr>
<tr>
<td>RR, 95% CI*</td>
<td>2.13, 1.09–6.78</td>
<td>1.16, 0.86–3.59</td>
</tr>
</tbody>
</table>

Nonhypertensive subjects (n=7632)

| I                             | 1.66 (30)  | 1.19 (35)  |
| II                            | 1.42 (24)  | 1.17 (33)  |
| III                           | 1.34 (22)  | 1.07 (22)  |
| P                             | 0.458      | 0.415      |
| RR, 95% CI*                   | 1.23, 0.84–3.89 | 1.11, 0.85–3.54 |

Numbers in parentheses in body of table indicate deaths. Rates are per 1000 person-years.

*P value and RR (95% CI) for III vs I were calculated using the Mantel-Haenszel test statistic.
higher stroke mortality rate compared with those with potassium intake >2584 mg/d.

Discussion

In this prospective study of the US population, increased dietary potassium intake was related to a lower stroke mortality only among black and hypertensive men and not among white or nonhypertensive men or women. These results are partly consistent with previous reports.

A protective effect of dietary potassium on risk of stroke was first reported by Khaw and Barrett-Connor. They examined the relationship between the 24-hour dietary potassium intake at baseline and subsequent stroke mortality. In a 12-year study, 24 stroke deaths were recorded among 859 men and women aged 50 to 79 years. Stroke-related mortality was significantly associated with a low potassium intake at baseline. The present study included nearly 13 times as many stroke deaths (304 versus 24) as the earlier study and had a 15% black population. The major difference between the 2 studies was the association of dietary potassium intake and stroke mortality among women. We did not confirm the association of dietary potassium intake and stroke mortality found by Khaw and Barrett-Connor among women in the NHANES data. In fact, the much stronger association among women than men in the study of Khaw and Barrett-Connor directly conflicts with our findings. The experience of blacks and hypertensives could not be explored in the study of Khaw and Barrett-Connor.

More recently, in the National Health Professionals Study, dietary potassium intake was assessed by a semiquantitative food frequency questionnaire. Among a total of 43,738 men who were health professionals, aged 40 to 75 years, without diagnosed cardiovascular disease or diabetes, 328 strokes were documented during 8 years of follow-up. In that study as well, potassium intake was inversely related to the risk of stroke. The inverse association of dietary potassium intake and stroke mortality was stronger in hypertensive than in normotensive men. The 24-hour dietary recall has been reported to be the most accurate method for dietary assessment, although food frequency methods are easy for subjects to complete and are widely used in epidemiological studies, and the validity of food frequency questionnaires has been validated by dietary recall measure. Men in the Health Professional Study can be assumed to have shared a homogeneous socioeconomic distribution, and therefore the study did not address the difference in association of dietary potassium and stroke mortality among blacks and whites.

Several other studies have also identified the presence of an inverse relationship between potassium intake and stroke mortality. However, these studies are limited by failing to account for dietary caloric intake. Xie et al. conducted an ecological study using mean 24-hour urinary potassium and sodium excretion from the INTERSALT study and age-standardized stroke mortality for 45- to 74-year-old men and women from 25 countries. A significant and inverse correlation was found between mean 24-hour urinary potassium excretion and stroke mortality.

The mechanism by which increased dietary potassium intake might prevent stroke is not known. It may be its hypotensive effect. In randomized trials, high potassium intake has caused modest reduction in blood pressure, especially among hypertensive subjects. Other mechanisms that have been suggested include inhibition of free radical formation, vascular smooth muscle proliferation, and arterial thrombosis. However, these effects have been produced by experimental increases in serum potassium concentrations in animals, and their relevance to dietary intake in humans is uncertain. High potassium intake may increase serum concentration, particularly when serum level is low or sodium intake is high, and could therefore reduce the risk of hypokalemia among men at high risk because of diuretic treatment. This may contribute to the protective effect in hypertensive men.

A particular association of dietary potassium intake and stroke mortality among black men is reported here for the first time. Dietary potassium intake was significantly lower among blacks than whites (1607 versus 2178 mg/d). Since the general level was low among blacks, perhaps the hypotensive effect of increased potassium intake may have been greater than in whites, who generally had higher potassium intakes. It may also reflect a threshold effect. The strong association in blacks, who consumed far less potassium and had higher...
blood pressures and a greater incidence of stroke, suggests an opportunity to further explore the health potential of increasing potassium intake among persons with low consumption. This study, as well as all earlier studies, is limited by the availability of only a single baseline dietary assessment of potassium and energy intake and by recall rather than objective measurement. Memory can be faulty, estimates of portion size can be mistaken, and diet can change from day to day. The single baseline measure of dietary potassium does not, of course, permit correction for regression dilution bias. Thus, the finding of associations probably underestimates the true relationships. Most probably the misclassification of baseline measurement was randomly distributed and would therefore tend to mute any real association between potassium intake and outcome. It should be noted, however, that other studies have shown that middle-aged subjects are likely to have a stable nutrient intake over many years.20,21 Other dietary factors, such as calcium and magnesium, might confound the association of dietary potassium and stroke mortality. In addition, in some subgroups, low statistical power might account for the lack of significant association between dietary potassium intake and stroke mortality. The large size of the NHANES population and its standardized methods, as well as standard codes adopted by the National Death Index, make it unlikely that directional bias has influenced these results. Moreover, the ability of dietary measures from NHANES I data to correlate with other outcomes has been previously demonstrated.22–24

In summary, findings in this general US population confirm an inverse association of dietary potassium intake with stroke mortality. However, after we controlled for other potential confounding factors, this association remained significant only among black men and hypertensive men. Further epidemiological follow-up studies, with large sample size, are necessary to confirm this association.

Acknowledgments

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References

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