Caffeinated beverage intake and the risk of heart disease mortality in the elderly: a prospective analysis¹,²

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ABSTRACT

Background: Motivated by the possibility that caffeine could ameliorate the effect of postprandial hypotension on a high risk of coronary events and mortality in aging, we hypothesized that caffeinated beverage consumption decreases the risk of cardiovascular disease (CVD) mortality in the elderly.

Objective: The objective of the study was to use prospective cohort study data to test whether the consumption of caffeinated beverages exhibits this protective effect.

Design: Cox regression analyses were conducted for 426 CVD deaths that occurred during an 8.8-y follow-up in the prospective first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. The analysis involved 6594 participants aged 32–86 y with no history of CVD at baseline.

Results: Participants aged ≥65 y with higher caffeinated beverage intake exhibited lower relative risk of CVD and heart disease mortality than did participants with lower caffeinated beverage intake. It was a dose-response protective effect: the relative risk (95% CI) for heart disease mortality was 1.00 (referent), 0.77 (0.54, 1.10), 0.68 (0.49, 0.94), and 0.47 (0.32, 0.69) for <0.5, 0.5–2, 2–4, and ≥4 servings/d, respectively (P for trend = 0.003). A similar protective effect was found for caffeine intake in mg/d. The protective effect was found only in participants who were not severely hypertensive. No significant protective effect was found in participants aged <65 y or in cerebrovascular disease mortality for those aged ≥65 y.

Conclusion: Habitual intake of caffeinated beverages provided protection against the risk of heart disease mortality among elderly participants in this prospective epidemiologic analysis. Am J Clin Nutr 2007;85:392–8.

KEY WORDS Aging, beverages, caffeine, cardiovascular disease, coffee, heart disease, mortality risk

INTRODUCTION

Previous epidemiologic studies of the relation between caffeinated beverage intake and the risk of cardiovascular disease (CVD) have yielded conflicting results (1–3). It is possible that the conflict is due to differences between nonelderly and elderly persons. One study found that coffee drinking increased the risk of CVD mortality in the elderly, whereas another study found a multiplicative effect of coffee and blood pressure (BP) on the risk of CVD mortality in the elderly.

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SUBJECTS AND METHODS

Database

Data from a prospective follow-up study, the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-Up Study (NHEFS), were used for the study.

Methods

NHANES I, a probability sample survey of the noninstitutionalized civilian US population, was conducted from 1971 to 1973 (11). The NHEFS is a follow-up study of those NHANES I participants aged 25–74 y (n = 14,407). NHEFS contains 4 follow-up surveys, conducted in 1982–1984, 1986, 1987, and 1992. The baseline data used in the current study were obtained by means of medical histories and examinations at the NHANES I survey and at the first follow-up survey in 1982–1984 (12).

Participants with any missing data and those with a self-reported history of CVD in 1982–1984 were excluded from the analyses. After exclusions, 6594 participants aged 32–86 y in the 1982–1984 survey remained for evaluation, along with 426 CVD deaths that occurred during the subsequent follow-up, which lasted an average of 8.8 y for censored participants.

Our procedures were in accordance with the ethical standards of our institution’s committee on human experimentation. We obtained approval for the use of the NHEFS data.
Mortality data

The study’s mortality data were obtained from the 1986, 1987, and 1992 surveys. Each death was confirmed by death certificate or proxy interview. Death certificates were obtained for >95% of deceased participants (13). Cause of death was determined from the death certificate and coded with the use of International Classification of Diseases Ninth Revision (ICD-9) categories (14). CVD mortality (ICD-9 codes 390–448) included rheumatic fever and rheumatic heart disease (codes 390–398); hypertensive heart disease (codes 401–404); ischemic heart disease (codes 410–414); diseases of the pulmonary circulation (codes 415–417); endocarditis, pericarditis, myocardiitis, mitral and aortic valve disorders, and heart failure (codes 420–429); cerebrovascular diseases (codes 430–438); and atherosclerosis, aortic aneurysm, and diseases of the arteries, arterioles, and capillaries (codes 440–448). Cerebrovascular mortality included intracranial hemorrhage (codes 431–432), cerebral thrombosis or occlusion (codes 434.0 and 434.9), cerebral embolism (code 434.1), and late effects of cerebrovascular diseases (codes 430, 433, and 435–438). Heart disease mortality included all noncerebrovascular CVD mortality.

Other variables

History of CVD and diabetes were based on participants’ responses to one question in the 1982–1984 survey. Each participant was asked whether a doctor had said the participant had the condition.

Body mass index in 1982–1984 was calculated as the body weight, measured in kilograms in 1982–1984, divided by the height squared, measured in meters in 1971–1975. Beverage intake was determined from 2 questions asked on a food-frequency questionnaire in 1982–1984. The first question pertained to the number of servings of the beverage usually consumed, and the second pertained to the time period during which the servings were consumed. These questions were used to ascertain the consumption levels of ground caffeinated coffee, ground decaffeinated coffee, regular tea, instant caffeinated coffee, instant decaffeinated coffee, herbal tea, and colas. Our main predictor was the intake of caffeinated beverages, defined as the total reported daily consumption (in cups; 1 cup = 177 mL) of ground caffeinated coffee, instant caffeinated coffee, and regular tea plus glasses or cans (1 glass or can = 355 mL) per day of colas (diet or regular). The following categories of caffeinated beverage intake were used in our analyses: <0.5, 0.5–2, 2–4, and ≥4 servings/d. The intake of decaffeinated beverages was defined as the total reported cups/d of ground decaffeinated coffee, instant decaffeinated coffee, and herbal tea. A variable representing an American-style diet and based on the work of van Dam et al (15) was also constructed from food-frequency data.

Daily caffeine intake was based on estimates of the caffeine content of servings of beverages and chocolate snacks. The estimates were derived from 2 literature reviews covering the follow-up period of our study, ie, 1982–1992 (16, 17). The estimates of caffeine content per serving were 159 mg for ground caffeinated coffee, 83 mg for instant caffeinated coffee, 42 mg for colas, 36 mg for regular tea, and 6 mg for chocolate snacks. The estimates were multiplied by the daily number of servings of each beverage and chocolate snack and then totaled for each subject. In the survival analyses, we used caffeine intake categories of <30, 30–100, 100–350, and ≥350 mg/d because they yielded approximately the same number of participants and events in each category as did our categories of caffeinated beverages.

Statistical analysis

The 1982–1984 survey was used as the baseline in all survival analyses. Cox proportional-hazards regression (18) was used to calculate the relative risks (RRs) of mortality at each level of beverage intake and to adjust the RRs for the effects of covariates. The –2 log likelihood ratio test was used to compare the fit of alternative models. Cumulative hazard and log minus log plots provided no evidence against proportionality assumptions (19).

Significance of the trend in RRs across levels of the predictor was assessed in analyses with the predictor as a continuous variable. The following covariates were used to adjust RRs in these survival analyses: age (nine 5-y categories from <50 to ≥85 y); smoking (never smoker, former smoker, <1 pack/d, or ≥1 pack/d); sex; race (white or nonwhite); per capita income (continuous variable); physical activity (5 categories); educational level (ordinal variable, 18 levels devised by NHEFS researchers); alcohol consumption (<1 serving/mo, 1 serving/mo, 1 serving/wk, ≤3 servings/d, or >3 servings/d); body mass index ([in kg/m²] <23, 23–26, 26–29, or ≥29); and American-style diet (quintiles).

Tests for statistical interaction found a significant interaction between caffeinated beverage intake and age (P = 0.02) and blood pressure (P = 0.001). Therefore, separate analyses were conducted in participants aged <65 and those aged ≥65 y. We chose an age of 65 y as the cutoff because this age is traditionally used to distinguish elderly from nonelderly persons. We also conducted separate analyses for different levels of BP. We created the BP subgroups by using the definitions of hypertension, prehypertension, and normal blood pressure in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (20). We used SPSS software (version 11.5; SPSS Institute, Chicago, IL) for statistical analyses.

RESULTS

Baseline characteristics

Of participants aged ≥65 y (Table 1) and <65 y (Table 2), those who consumed ≥4 servings/d were younger, had a higher American-style diet score, were more likely to be male and to smoke and were less likely to be taking antihypertensives than were those who consumed <4 servings/d. Increasing caffeinated beverage intake was associated with an increasing intake of caffeinated coffee, regular tea, and colas and a decreasing intake of ground decaffeinated coffee, instant decaffeinated coffee, and herb tea.

Cause of death, age, and type of cardiovascular disease

Higher caffeinated beverage intake was followed by lower RR of CVD mortality in a dose-response manner for participants aged ≥65 y (Table 3). The result was similar for heart disease mortality but not for cerebrovascular disease mortality. No significant relation was found between caffeinated beverage intake and the risk of CVD or heart disease mortality in participants aged <65 y. Only 12 cerebrovascular deaths occurred in participants aged <65 y; this number was too few for calculation of hazard ratios.

Caffeine

The analyses in Table 3 were repeated by using estimated caffeine intake (in mg/d) as the predictor. The results were very
TABLE 1
Characteristics of subjects aged ≥65 y with no reported history of cardiovascular disease at the follow-up baseline: the 1982-1984 survey in the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-Up Study

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>&lt;0.5 (n = 292)</th>
<th>≥0.5 to &lt;2 (n = 349)</th>
<th>≥2 to &lt;4 (n = 631)</th>
<th>≥4 (n = 441)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) (\dagger)</td>
<td>75.6 ± 0.5 (\pm 0.5)</td>
<td>76.0 ± 0.3 (\pm 0.3)</td>
<td>75.0 ± 0.2 (\pm 0.2)</td>
<td>73.7 ± 0.3 (\pm 0.3)</td>
</tr>
<tr>
<td>Men (%) (\dagger)</td>
<td>42.5</td>
<td>39.0</td>
<td>39.1</td>
<td>50.3</td>
</tr>
<tr>
<td>Per capita income ($)</td>
<td>7.52 ± 0.46 (\pm 0.46)</td>
<td>7.75 ± 0.42 (\pm 0.42)</td>
<td>7.41 ± 0.30 (\pm 0.30)</td>
<td>8.00 ± 0.34 (\pm 0.34)</td>
</tr>
<tr>
<td>Educational level (\dagger)</td>
<td>32.1 ± 0.4 (\pm 0.4)</td>
<td>31.8 ± 0.4 (\pm 0.4)</td>
<td>31.8 ± 0.2 (\pm 0.2)</td>
<td>32.3 ± 0.3 (\pm 0.3)</td>
</tr>
<tr>
<td>Current smoker (%) (\dagger)</td>
<td>12.7</td>
<td>10.0</td>
<td>13.5</td>
<td>23.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.4</td>
<td>23.8</td>
<td>28.8</td>
<td>31.5</td>
</tr>
<tr>
<td>Physical activity (\dagger)</td>
<td>3.72 ± 0.06 (\pm 0.06)</td>
<td>3.68 ± 0.06 (\pm 0.06)</td>
<td>3.75 ± 0.05 (\pm 0.05)</td>
<td>3.90 ± 0.05 (\pm 0.05)</td>
</tr>
<tr>
<td>American-style diet (\dagger)</td>
<td>24.9 ± 0.9</td>
<td>26.5 ± 0.8</td>
<td>27.2 ± 0.6</td>
<td>31.2 ± 0.8</td>
</tr>
<tr>
<td>Taking antihypertensives (%) (\dagger)</td>
<td>38.7</td>
<td>37.8</td>
<td>38.5</td>
<td>29.3</td>
</tr>
<tr>
<td>History of diabetes (%)</td>
<td>8.2</td>
<td>10.1</td>
<td>8.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic (mm Hg)</td>
<td>141.0</td>
<td>76.8 ± 0.7</td>
<td>76.0 ± 0.6</td>
<td>75.3 ± 0.5</td>
</tr>
<tr>
<td>Diastolic (mm Hg)</td>
<td>141.0</td>
<td>141.0</td>
<td>142.3 ± 1.2</td>
<td>141.1 ± 0.8</td>
</tr>
<tr>
<td>Taking antihypertensives (%) (\dagger)</td>
<td>38.7</td>
<td>37.8</td>
<td>38.5</td>
<td>29.3</td>
</tr>
<tr>
<td>History of diabetes (%)</td>
<td>8.2</td>
<td>10.1</td>
<td>8.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Beverage consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ground caffeinated coffee (cups/d) (\dagger)</td>
<td>0.00 ± 0.00</td>
<td>0.26 ± 0.02</td>
<td>1.00 ± 0.04</td>
<td>2.63 ± 0.14</td>
</tr>
<tr>
<td>Instant caffeinated coffee (cups/d) (\dagger)</td>
<td>0.00 ± 0.00</td>
<td>0.22 ± 0.02</td>
<td>0.49 ± 0.03</td>
<td>0.91 ± 0.08</td>
</tr>
<tr>
<td>Regular tea (cups/d) (\dagger)</td>
<td>0.08 ± 0.01</td>
<td>0.38 ± 0.02</td>
<td>0.61 ± 0.03</td>
<td>0.99 ± 0.07</td>
</tr>
<tr>
<td>Colas (cans/d) (\dagger)</td>
<td>0.06 ± 0.01</td>
<td>0.21 ± 0.02</td>
<td>0.27 ± 0.02</td>
<td>0.42 ± 0.04</td>
</tr>
<tr>
<td>Ground decaffeinated coffee (cups/d) (\dagger)</td>
<td>0.45 ± 0.08</td>
<td>0.18 ± 0.04</td>
<td>0.08 ± 0.02</td>
<td>0.06 ± 0.02</td>
</tr>
<tr>
<td>Instant decaffeinated coffee (cups/d) (\dagger)</td>
<td>1.43 ± 0.07</td>
<td>0.78 ± 0.05</td>
<td>0.45 ± 0.04</td>
<td>0.34 ± 0.04</td>
</tr>
<tr>
<td>Herb tea (cups/d) (\dagger)</td>
<td>0.07 ± 0.02</td>
<td>0.07 ± 0.02 (\pm 0.02)</td>
<td>0.04 ± 0.01 (\pm 0.01)</td>
<td>0.02 ± 0.01 (\pm 0.01)</td>
</tr>
<tr>
<td>Beverage consumers (% of subjects)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ground caffeinated coffee (\dagger)</td>
<td>0.0</td>
<td>29.8</td>
<td>61.7</td>
<td>83.0</td>
</tr>
<tr>
<td>Instant caffeinated coffee (\dagger)</td>
<td>4.1</td>
<td>29.5</td>
<td>33.4</td>
<td>36.5</td>
</tr>
<tr>
<td>Regular tea (\dagger)</td>
<td>48.6</td>
<td>69.6</td>
<td>71.0</td>
<td>72.1</td>
</tr>
<tr>
<td>Colas (\dagger)</td>
<td>39.7</td>
<td>58.2</td>
<td>58.6</td>
<td>66.0</td>
</tr>
<tr>
<td>Ground decaffeinated coffee (\dagger)</td>
<td>99.3</td>
<td>63.3</td>
<td>36.9</td>
<td>27.3</td>
</tr>
<tr>
<td>Instant decaffeinated coffee (\dagger)</td>
<td>83.9</td>
<td>58.2</td>
<td>34.2</td>
<td>24.9</td>
</tr>
<tr>
<td>Herb tea (\dagger)</td>
<td>14.8</td>
<td>14.4</td>
<td>9.5</td>
<td>6.4</td>
</tr>
</tbody>
</table>

\(\dagger\) Differences between serving groups were tested by using a chi-square test for dichotomous variables and ANOVA with Tamhane’s post hoc test for continuous variables. Values in a row with different superscript letters are significantly different, \(P < 0.05\).

Servings of caffeinated beverages were defined as the total reported cups/d of ground caffeinated coffee, instant caffeinated coffee, and regular tea plus glasses or cans/d of colas (diet or regular).

\(\dagger\) \(P < 0.001\).

\(\dagger\) \(P < 0.01\).

\(\dagger\) \(P < 0.05\).

\(\dagger\) An ordinal variable with 18 values between 10 and 45, assigned by NHANES researchers. Higher values represented higher levels of education.

\(\dagger\) Five levels (2–6) of physical activity were calculated as the sum of the self-reported estimates of the level of recreational (1–3) and regular daily (1–3) activities. Higher values represented higher levels of physical activity.

\(\dagger\) American-style diet based on food-frequency data, as described in Methods. Higher values represented diets closer to an American-style diet.

similar to those for caffeinated beverage intake. For instance, in participants aged ≥65 y, the RR of heart disease mortality were 1.00 (referent), 0.77 (0.55, 1.20), 0.69 (0.50, 0.94), and 0.56 (0.39, 0.8) for <30, 30–100, 100–350, and ≥350 mg caffeine/d, respectively (\(P = 0.018\)). The addition of caffeine intake to the model containing caffeinated beverage intake and of caffeinated beverage intake to the model containing caffeine intake did not significantly improve those models (\(P = 0.94\) and 0.09, respectively).

No evidence was found that decaffeinated beverages provided a protective effect. In participants aged ≥65 y, the RR for heart disease mortality were 1.00 (referent), 0.92 (0.68, 1.26), 0.93 (0.61, 1.43), and 0.94 (0.62, 1.43) for 0, 0–1, 1–2, and ≥2 servings decaffeinated beverages/d, respectively (\(n = 1703;\) deaths = 280; \(P\) for trend = 0.915).

**Different levels of blood pressure**

No significant protective effect was found in participants aged ≥65 y with stage 2 hypertension (Table 4). A significant protective effect was found in participants with stage 1 hypertension and in those with prehypertension or normal BP.

**Secondary analyses**

The analyses of CVD and heart disease mortality in participants aged ≥65 y (see Table 3) were repeated \(I\) without excluding participants with no history of CVD; \(2\) in participants not on...
antihypertensive medications; 3) with the use of diastolic BP, systolic BP, self-rated health, and a history of diabetes as covariates; and 4) with the use of 0 and 0–1 servings caffeinated beverages/d as the referent category. These analyses yielded essentially the same pattern of results as in Table 3. For instance, after inclusion of participants with a history of CVD, the RRs (95% CI) for heart disease mortality were 1.00 (referent), 0.84 (0.65, 1.09), 0.66 (0.52, 0.83), and 0.52 (0.39, 0.69) for <0.5, 0.5–2, 2–4, and ≥4 servings caffeinated beverages/d, respectively (P for trend = 0.003). The numbers of events and participants in the referent category were 28 and 93, respectively.

The analyses in Table 4 were repeated with diastolic BP, systolic BP, use of hypertensive medication, self-rated health, and a history of diabetes as covariates. The results showed the same patterns as those in Table 4.

The analysis in Table 3 of heart disease mortality in participants aged ≥65 y was repeated by using the intake of individual beverages as predictors. We used 0, 0–2, and ≥2 servings/d as the intake categories for all beverages except herb tea. For herb tea, few events occurred in the category of ≥2 servings/d, so we used 0, 0–1, and ≥1 servings/d. A significant protective effect was found for ground...
Relative risk (95% CI) for cardiovascular disease (CVD), heart disease, and cerebrovascular mortality by level of caffeinated beverage intake in different age groups in the 8.8-y follow-up starting at the 1982-1984 survey in the first National Health and Nutrition Examination Survey Epidemiologic Follow-Up Study.

<table>
<thead>
<tr>
<th>Person-years of follow-up</th>
<th>Subjects</th>
<th>No. of deaths</th>
<th>Servings of caffeinated beverage per day</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;0.5</td>
<td>≥0.5 to &lt;2</td>
</tr>
<tr>
<td>≥65 y old CVD mortality</td>
<td>12,793</td>
<td>1713</td>
<td>349</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Heart disease mortality</td>
<td>12,793</td>
<td>1713</td>
<td>282</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>12,793</td>
<td>1711</td>
<td>67</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>&lt;65 y old CVD mortality</td>
<td>43,417</td>
<td>4881</td>
<td>77</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Heart disease mortality</td>
<td>43,417</td>
<td>4881</td>
<td>65</td>
<td>1.00 (Referent)</td>
</tr>
</tbody>
</table>

1 Relative risks calculated by using Cox regression and adjusted for age, smoking, BMI, sex, race, physical activity, alcohol consumption, per capita income, educational level, and American-style diet, as described in Methods.
2 A serving of caffeinated beverages was 1 cup of ground caffeinated coffee, instant caffeinated coffee, or regular tea or a glass or can of cola (diet or regular).
3 P < 0.05.
4 P < 0.001.
5 Only 12 cerebrovascular disease deaths occurred in participants <65 y old, and that was too few deaths for hazard ratios to be calculated.

Table 4 Relative risk (95% CI) for heart disease mortality by level of caffeinated beverage intake in subjects aged ≥65 y in the 8.8-y follow-up starting at the 1982-1984 survey in the first National Health and Nutrition Examination Survey Epidemiologic Follow-Up Study.

<table>
<thead>
<tr>
<th>Person-years of follow-up</th>
<th>Subjects</th>
<th>No. of deaths</th>
<th>Hazard ratios for daily servings of caffeinated beverages</th>
<th>Blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;1.5</td>
<td>≥1.5</td>
</tr>
<tr>
<td>Stage 2 hypertensives 3</td>
<td>2137</td>
<td>290</td>
<td>59</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Stage 1 hypertensives 4</td>
<td>3981</td>
<td>512</td>
<td>88</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Prehypertensives and normotensives 6</td>
<td>6215</td>
<td>821</td>
<td>112</td>
<td>1.00 (Referent)</td>
</tr>
</tbody>
</table>

1 Relative risks calculated by using Cox regression and adjusted for age, smoking, BMI, sex, race, physical activity, alcohol consumption, per capita income, educational level, and American-style diet, as described in Methods. Hypertension, prehypertension, and ideal blood pressure are as defined in the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (20).
2 A serving of caffeinated beverages was 1 cup of ground caffeinated coffee, instant caffeinated coffee, or regular tea or a glass or can of cola (diet or regular).
3 Systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 100 mm Hg.
4 ± SEM (all such values).
5 Systolic blood pressure 140–159 mm Hg or diastolic blood pressure 90–99 mm Hg.
6 P < 0.05.
7 Systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg.
DISCUSSION

Our main finding was that, in the prospective NHEFS cohort, participants aged \( \geq 65 \) y without stage 2 hypertension who reported a higher intake of caffeinated beverages experienced a lower risk of HD mortality than did those who reported a lower intake. The association was dose related, and it was a substantial effect, in that \( \geq 4 \) servings caffeinated beverage/d were associated with a significant (53%) decrease in the risk of heart disease mortality. Secondary analyses showed a similar protective effect whether participants with a history of CVD were excluded or not. Similar results were also found in analyses that adjusted for BP, antihypertensive medication usage, a history of diabetes, and self-rated health. The protective effect was stronger when the referent category was 0 than when it was \(< 0.5 \) servings/d.

If our findings are confirmed, they may have important ramifications because caffeinated beverages are widely consumed, and heart disease is one of the leading causes of death in the elderly. In a survey, \( \approx 80\% \) of US adults aged \( >50 \) y reported coffee consumption, and \( 40\% \) reported tea consumption (21). Heart disease deaths among persons aged \( >65 \) y represented \( >80\% \) of all heart disease deaths in the United States in 2002 (22; see Table 31), and the cost of treating heart disease was estimated to be \$148 billion in 2006 (23; see Table 14A).

Our results do not allow us to conclude whether caffeine or the caffeinated beverages were responsible for the protective effect. Three of our findings suggest that caffeine is a possible causal agent. First, we found that the total caffeine intake (in mg/d) yielded a protective effect similar to that of the number of daily servings of caffeinated beverages. Second, we found no significant protective effect from decaffeinated beverages, individually or when they were combined. Third, we found a protective effect only for the 2 caffeinated beverages with relatively larger proportions of caffeine per serving—ground caffeinated coffee and instant caffeinated coffee. The lack of a significant effect for regular tea and colas could be due to the lower caffeine content of these beverages as compared with that of the caffeinated coffees. The fact that the protective effect increased with an increasing number of servings of caffeinated beverages/d suggests that a greater number of coffee doses per day provides more protection against heart disease. The half-life of caffeine in the body is \( \approx 3–7 \) h (21), and its effects diminish substantially within \( \approx 3 \) h (24). It seems possible, therefore, that the consumption of a greater number of doses of caffeine per day would be more likely to provide continuous protection during a person’s waking hours. This possibility is consistent with the idea that caffeine protects against heart disease in the elderly by inducing a pressor effect that increases blood pressure and hence counteracts the effects of postprandial hypotension.

Overall, our findings do not allow for a conclusion as to whether caffeine ingestion protects against heart disease mortality by inducing blood pressure increases that counteract postprandial hypotension. However, some evidence supports this hypothesis. First, the pressor effect is greater in elderly than in young adults (8, 10). Second, diastolic and mean arterial BP tend to decrease with age in persons aged \( >70 \) y (25). Third, although humans develop tolerance to the pressor effect, tolerance decreases with increasing age (9), and thus tolerance may not be complete in the elderly (26).

In contrast, reasons exist not to believe that an amelioration of the negative cardiovascular effects of postprandial hypotension by a pressor effect explains our findings. First, we found no protective effect for cerebrovascular disease, and it is conceivable that a pressor effect should help protect the cerebrovascular circulation against low BP. Second, we found no significant protective effect for elderly stage 2 hypertensives, and elderly hypertensives have been found to exhibit greater postprandial postprandial decreases in BP than do age-matched normotensives (5).

It is also possible that our findings are caused by one (or more) of caffeine’s many effects in the cardiovascular system (27). Our finding that a protective effect existed for those aged \( \geq 65 \) y but not for those aged \(< 65 \) y could result from the fact that the causal changes induced by caffeine accumulate over time, and manifest as lower heart disease risk starting at \( \approx 65 \) y of age. Such changes include caffeine’s demonstrated abilities to increase myocardial contractility (28), reduce fibrinolysis time (29), increase plasma renin activity (24), inhibit baroreflex activity (30), act as a diuretic (21), alter electroencephalogram wave patterns (31), and mobilize intracellular calcium (32). It is also possible that the causal changes induced by caffeine are more pronounced in the elderly than in younger persons (21). Caffeine is found in coffee, tea, cocoa, and chocolate, all of which contain compounds such as antioxidants and flavonoids. It is possible that these compounds, which have been shown to preserve cardiovascular function in some studies (33), are part of the explanation for our findings.

We found a significant negative association between the risk of heart disease mortality and caffeinated beverage intake in the 1713 subjects aged \( \geq 65 \) y but not in the 4881 NHEFS participants aged \(< 65 \) y. Differing proportions of participants aged \( \geq 65 \) y may therefore explain some of the conflicting findings in previous analyses. For instance, our results suggest that it is possible that Andersen et al (3) may have found a stronger protective effect for caffeinated coffee if their cohort had included a higher proportion of participants aged \( >65 \) y. It is difficult to compare our results with previous prospective epidemiologic results for caffeinated beverages and CVD mortality. First, few such previously published analyses were conducted in persons aged \( \geq 65 \) y. Second, most previous studies that used follow-up cohorts containing persons aged \( \geq 65 \) y did not distinguish between caffeinated and decaffeinated beverages. Lindsted et al (4) did find a negative association between coffee consumption and the risk of CVD mortality in older participants in a 26-y follow-up—a finding that is consistent with our main finding.

The current study has several limitations. First, generalization of these findings to the overall US population is hindered because the RRs were not based on a random sample of the US population—mainly because 1647 of the original 14 407 NHANES I participants died between 1971–1975 and 1982–1984, the baseline in the present survival analyses. Second, we were not able to include caffeine intake from medications, such as aspirin, that contain caffeine, because data on quantities and frequency of usage of such medications are not available in the NHEFS. Third, we did not have data to distinguish between caffeinated and decaffeinated colas. It seems unlikely that this latter limitation had a major effect on our findings, for several reasons: 1) colas represented only 1 of 4 caffeinated beverages in our study; 2) colas had a substantially smaller caffeine content per serving than did the caffeinated coffees; and 3) participants consumed fewer daily servings of colas than of the other caffeinated beverages. Fourth, the current study was an epidemiologic study and does
not prove a cause-and-effect relation. This study does not provide a valid basis for recommending increased consumption of caffeinated beverage. Our findings require confirmation in future epidemiologic, metabolic, and clinical trial studies.

In conclusion, our analysis of the prospective NHEFS data showed that habitual intake of caffeinated beverages provides strong protection against the risk of heart disease mortality. This finding was obtained only in nonhypertensive elderly participants.

The original source of the NHEFS data is the National Center for Health Statistics (NCHS); the Inter-University Consortium on Political and Social Research (ICPSR) provided the data. Neither NCHSR nor ICPSR is responsible for this report, which is the work of the authors, who appreciate being able to obtain and work with the data.

JAG planned the study; RS reviewed the literature on the caffeine content of the caffeinated beverages studies; JAG conducted the statistical analyses; JAG wrote the manuscript; and JAG, CCD, JK, RK, and SK contributed to revisions of the manuscript. We appreciate the constructive comments of several anonymous Journal reviewers, which helped us improve the manuscript. None of the authors had any personal or financial conflict of interest.

REFERENCES