Coffee Intake and Risk of Hypertension

The Johns Hopkins Precursors Study

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Background: Whether the increase in blood pressure with coffee drinking seen in clinical trials persists over time and translates into an increased incidence of hypertension is not known.

Methods: We assessed coffee intake in a cohort of 1017 white male former medical students (mean age, 26 years) in graduating classes from 1948 to 1964 up to 11 times over a median follow-up of 33 years. Blood pressure and incidence of hypertension were determined annually by self-report, demonstrated to be accurate in this cohort.

Results: Consumption of 1 cup of coffee a day raised systolic blood pressure by 0.19 mm Hg (95% confidence interval, 0.02-0.35) and diastolic pressure by 0.27 mm Hg (95% confidence interval, 0.15-0.39) after adjustment for parental incidence of hypertension and time-dependent body mass index, cigarette smoking, alcohol drinking, and physical activity in analyses using generalized estimating equations. Compared with nondrinkers at baseline, coffee drinkers had a greater incidence of hypertension during follow-up (18.8% vs 28.3%; P = .03). Relative risk (95% confidence interval) of hypertension associated with drinking 5 or more cups a day was 1.35 (0.87-2.08) for baseline intake and 1.60 (1.06-2.40) for intake over follow-up. After adjustment for the variables listed above, however, these associations were not statistically significant.

Conclusion: Over many years of follow-up, coffee drinking is associated with small increases in blood pressure, but appears to play a small role in the development of hypertension.

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A LINK BETWEEN coffee drinking and increased blood pressure has been postulated for at least 60 years. Administration of coffee has been demonstrated to raise blood pressure acutely, but adaptation to the cardiovascular effects of coffee drinking occurs quickly. A recent meta-analysis of 11 clinical trials with a median duration of 56 weeks, however, demonstrated a persistent relationship between coffee intake and an increase in blood pressure. No prospective studies of coffee drinking and risk of developing hypertension have been performed. Such studies are necessary to determine if the pressor effect of coffee drinking seen in clinical trials is maintained over time and whether it translates into an increased risk of developing hypertension over the long-term. We examined the long-term effect of coffee drinking on blood pressure and risk of hypertension in The Johns Hopkins Precursors Study, a prospective longitudinal study of former medical students. The availability of repeated measures of coffee intake from young adulthood to age 60 years, as well as validated self-reports of blood pressure and hypertension, offers a unique opportunity to address this important issue.

RESULTS

Characteristics of the men in medical school and during follow-up are displayed in Table 1. Eighty-two percent drank coffee. The median category of coffee drinking was 1 to 2 cups per day with a median intake of 2 cups per day among drinkers. The men were young, with desirable mean levels of body mass, systolic and diastolic blood pressure, and serum cholesterol. The heaviest coffee drinkers tended to be slightly older than the men who drank less or no coffee. Men who drank more coffee were more likely to drink alcohol and smoke cigarettes. Coffee intake in medical school was not related to physical activity, body mass index, or blood pressure at baseline.
PARTICIPANTS AND METHODS

STUDY POPULATION AND MEASUREMENTS

The Johns Hopkins Precursors Study was designed and initiated in 1947 by the late Caroline Bedell Thomas. The 1337 students who matriculated into the graduating classes of 1948 to 1964 of The Johns Hopkins University School of Medicine were eligible for the study. Between 1948 and 1964, 1160 male and 111 female students (95% of those eligible) were enrolled. In medical school, participants completed questionnaires about their medical history, family history of hypertension, health habits, and dietary habits including coffee intake and cigarette smoking. Participants also underwent a standardized medical examination that included measurement of weight, height, blood pressure, and total serum cholesterol. Blood pressure was assessed on multiple occasions (median of 9 measurements) in medical school using a standardized protocol. For the present analysis, the mean level of all measurements was used to estimate blood pressure at baseline.

Women were excluded from this analysis because of their small numbers. Seventeen men with average systolic blood pressure of 140 mm Hg or higher or diastolic blood pressure of 90 mm Hg or higher in medical school were also excluded. The remaining 1017 white men who provided coffee information in medical school are the study population for the present analysis.

ASSESSMENT OF COFFEE CONSUMPTION

Usual coffee intake was assessed up to 11 times: in medical school, every 5 years after graduation until 1984; and in 1978, 1986, 1989, and 1993. Information on cups of coffee consumed per day in medical school, in 1978 and later was obtained in response to an open-ended question. At the 5-year follow-ups, participants indicated their current intake based on 8 possible responses ranging from 0 to 7 or more cups a day. After 1986, participants were asked specifically about caffeinated coffee. Only information on caffeinated coffee was included in the analyses.

FOLLOW-UP PROCEDURES

Information on cigarette smoking, body weight, physical activity, and alcohol intake was obtained at baseline and at the same time points during follow-up as coffee drinking. Self-reports of smoking behavior and body weight have been validated in this cohort.

Methods of assessment of physical activity and alcohol intake varied over follow-up. Physical activity was assessed in medical school and over follow-up using the question, “How much physical training have you had in the past month?” Possible responses were none, little, moderate, and much. In 1978, 1986, 1989, and 1993, participants were asked the number of times per week that they engaged in physical activity vigorous enough to work up a sweat. Based on data from the years in which both questionnaires were administered, all responses were categorized based on the number of times per week the participants worked up a sweat. Alcohol intake was assessed in medical school, and every 5 years after graduation until 1984 by asking, “How much do you drink?” Possible responses were “never,” “occasional,” “varies,” and “regular.” In 1978, 1986, and later, a quantity-frequency measure of alcohol consumption was administered. Based on data from years when both questions were asked, alcohol intake from all questionnaires were converted to a quantity-frequency scale. Responses to both questions have been strongly related to the incidence of hypertension in this cohort. Prevalence of hypertension in parents was assessed at baseline and incidence of hypertension in parents was assessed annually after graduation.

Blood pressure after graduation was assessed by means of annual questionnaires. Participants were asked to measure their blood pressure in a seated position. The average number of years that participants reported their blood pressure was 11, with a range from 1 (n=39) to 27. Self-reports of blood pressure in a subset of this cohort have been found to be remarkably accurate. The correlation between measured and reported blood pressure was 0.67 for systolic blood pressure and 0.56 for diastolic blood pressure.

### Table 1. Characteristics of 1017 White Men Assessed in Medical School by Baseline Coffee Intake: The Johns Hopkins Precursors Study*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total</th>
<th>0</th>
<th>1-2</th>
<th>3-4</th>
<th>&gt;5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%) of men</td>
<td>1017 (100)</td>
<td>184 (18.1)</td>
<td>462 (45.4)</td>
<td>239 (23.5)</td>
<td>122 (13.0)</td>
</tr>
<tr>
<td>Age at graduation, y</td>
<td>26.3 (2.4)</td>
<td>26.2 (2.3)</td>
<td>26.1 (2.3)</td>
<td>26.2 (2.0)</td>
<td>27.4 (2.9)†</td>
</tr>
<tr>
<td>Alcohol, drinks/wk</td>
<td>6.6 (4.0)</td>
<td>4.6 (3.5)</td>
<td>6.4 (3.8)</td>
<td>7.4 (3.9)</td>
<td>8.3 (4.3)†</td>
</tr>
<tr>
<td>Vigorous exercise per week</td>
<td>0.8 (1.0)</td>
<td>0.9 (1.1)</td>
<td>0.8 (1.1)</td>
<td>0.6 (0.9)</td>
<td>0.8 (1.0)</td>
</tr>
<tr>
<td>Coffee intake, cups/d</td>
<td>2.3 (1.8)</td>
<td>0.0 (0)</td>
<td>1.5 (0.5)</td>
<td>3.4 (0.5)</td>
<td>5.9 (0.6)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.1 (2.5)</td>
<td>22.9 (2.4)</td>
<td>23.1 (2.3)</td>
<td>23.3 (3.0)</td>
<td>23.2 (2.7)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>115 (8.7)</td>
<td>115 (8.7)</td>
<td>115 (9.3)</td>
<td>115 (7.8)</td>
<td>116 (8.3)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>70 (6.5)</td>
<td>69 (6.3)</td>
<td>69 (6.3)</td>
<td>70 (6.3)</td>
<td>69 (6.4)</td>
</tr>
<tr>
<td>Cigarette smokers, No. (%)</td>
<td>493 (48)</td>
<td>41 (22)</td>
<td>204 (44)</td>
<td>145 (61)</td>
<td>103 (78)†</td>
</tr>
</tbody>
</table>

*Data are given as mean (SD) unless otherwise specified.
†P<.001, from analysis of variance and χ² analysis.

The total number of blood pressure measurements reported were 21457 and these were averaged to yield 11666 annual mean blood pressure estimates. Coffee drinking was reported within the previous 2 years for 7768 and these were included in the GEE analysis. Table 2 summarizes the results of the unadjusted GEE analysis. In analyses using coffee drinking as a continuous variable, 1 cup of coffee per day was associated with...
The annual questionnaires also asked about a diagnosis of and treatment for hypertension. A diagnosis of hypertension was assigned after review of annual questionnaires, blood pressure reports, and medical records by a committee of 5 internists trained in epidemiology without knowledge of the participant’s coffee intake. The committee’s criteria for hypertension were a reported blood pressure greater than or equal to 160/95 mm Hg on 1 annual questionnaire, greater than or equal to 140/90 mm Hg on 2 or more annual questionnaires, or hypertension requiring drug therapy. In those who met the criteria for hypertension, onset was defined as first reported elevated reading. The present analysis was based on events reported through December 31, 1995, representing a median follow-up of 33 years. Yearly response rates varied from 68% to 78%, with 87% to 94% of the cohort responding at least once during each 5-year period. Vital status of nonrespondents was ascertained by contacting family members, scanning obituaries, and searching the National Death Index. Vital status was known for greater than 99% of the cohort.

STATISTICAL ANALYSIS

The association of coffee drinking and blood pressure was assessed in longitudinal data analysis using the generalized estimating equations (GEE) approach developed by Liang and Zeger. The GEE accounts for correlation of blood pressure within individuals over time, allowing valid inferences from longitudinal data. For this analysis, coffee intake was parameterized as a continuous variable: 0 to 7 cups per day. The participants often reported more than 1 blood pressure reading on an annual questionnaire, so the mean of all blood pressures reported was used in the analysis. Blood pressures within 2 years after a report of coffee consumption were assigned to that measure of coffee intake. The number of years in which coffee intake was assessed was fewer than the number of years that blood pressure was reported. Blood pressure values were excluded from the analysis if data on coffee intake were not available within the prior 2 years. Observations were censored once a participant met the criteria for hypertension.

The cumulative incidence of subsequent hypertension associated with coffee intake at baseline was calculated for 4 categories of coffee consumption: none, 1 to 2 cups daily, 3 to 4 cups daily, and 5 or more cups daily, using Kaplan-Meier analysis.11 The difference in hypertension incidence between coffee intake levels was tested using the log-rank test.12 Age was the time variable used in all survival analyses. Coffee drinking was also modeled as a time-dependent categorical variable in Cox proportional hazards analysis.13 In these analyses, coffee consumption was defined by the level of most recent coffee intake prior to the first report of elevated blood pressure among those with hypertension in comparison with coffee consumption at the same age among those without elevated blood pressure. Multivariate Cox proportional hazards models were developed to adjust for possible confounding variables including incidence of hypertension in parents as well as time-dependent data during follow-up on number of cigarettes smoked, body mass index, physical activity, and alcohol intake. The models were stratified by calendar time periods to adjust for potential differences in baseline risk factors over time and possible secular trends in hypertension risk. Persons with missing data were excluded from the multivariate analysis. To examine the hypothesis that risk of hypertension varied by method of coffee preparation, calendar time was also used as a surrogate for preparation method.14 Time-dependent coffee intake was modeled as 3 calendar time-specific variables: before 1975, 1975 to 1984, and after 1984. These cut points were chosen because methods of coffee preparation began to shift toward use of automatic drip coffee makers around 1975, and a report on the relation of coffee drinking to coronary heart disease incidence in this cohort was published in 1984.14 Because coffee drinking has been suggested to interact with cigarette smoking to increase blood pressure,15 analyses were also performed within strata of lifetime smoking status. Estimates of relative risk and corresponding 2-sided 95% confidence intervals (CIs) relating coffee consumption to risk of hypertension were computed from the Cox models. All tests of significance were 2-tailed with an α level of .05.

Table 2. Unadjusted Mean Blood Pressure During a Median Follow-up of 33 Years by Coffee Consumption Over Follow-up: Generalized Estimating Equations Analysis

<table>
<thead>
<tr>
<th>Cups per Day</th>
<th>Mean (SE) Blood Pressure, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
</tr>
<tr>
<td>0</td>
<td>121.3 (0.5)</td>
</tr>
<tr>
<td>1-2</td>
<td>121.3 (0.3)</td>
</tr>
<tr>
<td>3-4</td>
<td>121.9 (0.3)</td>
</tr>
<tr>
<td>≥5</td>
<td>122.2 (0.4)</td>
</tr>
</tbody>
</table>

a 0.21 mm Hg (95% CI, 0.03-0.38 mm Hg; P=.02) higher systolic and 0.26 mm Hg (95% CI, 0.14-0.38; P<.001) higher diastolic pressure. After adjustment for age, cigarette smoking, incidence of hypertension in the participants’ mother and father, as well as changes in alcohol intake, physical activity, and body mass index during follow-up, the effect of coffee intake on systolic and diastolic blood pressure was similar and remained highly significant. In multivariate analyses, consumption of 1 cup of coffee a day increased systolic blood pressure by 0.19 mm Hg (95% CI, 0.02-0.35) and diastolic pressure by 0.27 mm Hg (95% CI, 0.15-0.39). There were no statistically significant interactions in the association of coffee drinking with blood pressure for cigarette smoking or any of the other variables included in the multivariate analysis.

During a median follow-up of 33 years, 281 men developed hypertension at a median age of 53 years. The unadjusted incidence of hypertension was 26.5% at age 60 years and 51.7% at age 77 years. Hypertension incidence varied by level of coffee intake (Figure). Estimates of incidence at the end of follow-up were highly variable because the staggered enrollment over 17 years resulted in a small number of men with follow-up to age 70 years. Thus, incidence rates at age 60 years are given in Table 3. The incidence of hypertension by age 60 years was greater in men who drank coffee in medical school (28.3%) than in those who did not (18.8%) (log-rank P=.03). Hypertension incidence increased progres-
sively in men drinking 1 to 2 cups a day and 3 to 4 cups a day compared with non–coffee drinkers (Table 3). In the heaviest coffee consumption group, however, incidence of hypertension fell to 25.8%, less than that in the 1 to 2 cups a day group.

Results of Cox proportional hazards analysis assessing the risk of hypertension associated with coffee drinking at baseline and during follow-up are given in Table 4. Compared with men who did not drink coffee at baseline, the relative risk of hypertension was greater in all categories of coffee drinking but relative risk estimates increased only slightly with successive levels of coffee drinking, and, as in the Kaplan-Meier analysis, decreased somewhat in the heaviest drinkers. Risk of hypertension was statistically significantly greater in those drinking 3 to 4 cups a day compared with the men who abstained. After taking into account differences among coffee intake categories in incidence of hypertension in parents and the number of cigarettes smoked, alcohol intake, physical activity, and body mass index during follow-up, the association of coffee drinking with hypertension incidence was not statistically significant. When coffee drinking in closer proximity to the onset of hypertension was examined by modeling coffee intake during follow-up as a time-dependent covariate, results were similar to those seen for baseline coffee intake.

In analyses stratified by smoking status at baseline, the unadjusted relative risk of hypertension associated with drinking 5 or more cups of coffee a day (modeled as a continuous variable) was similar for smokers (relative risk, 1.69; 95% CI, 1.35-2.03) and nonsmokers (relative risk, 1.45; 95% CI, 0.93-2.25) alike, providing no evidence of effect modification of an association of coffee drinking with hypertension by cigarette smoking status. Likewise, risk of hypertension associated with coffee intake did not differ by calendar time of assessment of coffee intake. The unadjusted relative risk of hypertension associated with drinking 5 cups of coffee per day was 1.54 (95% CI, 0.99-2.38) before 1975, 1.16 (95% CI, 0.71-1.88) between 1975 and 1984, and 1.10 (95% CI, 0.63-1.91) after 1984 (P for interaction = .21). Results were unchanged in multivariate analyses.

**COMMENT**

In this long-term prospective study, drinking 1 cup of coffee a day was associated with small increases in blood pressure. Despite this persistent pressor effect, long-term coffee drinking did not substantially increase the risk of developing hypertension in this cohort. Non-drinkers were at lower risk of hypertension than coffee drinkers but there was no progressive increase in risk as-
Most Recent Intake

who decreased their coffee intake experienced a fall in ing and blood pressure of which we are aware, persons
selton Study, the only prospective study of coffee drink-
sure is less than that seen in clinical trials. In the Bus-
tin continued adaptation over the long period of follow-up in
J-shaped associations may result from selective de-
alcohol intake, physical activity, and body mass index.

The lower risk of hypertension in the heaviest cof-
fee drinkers at baseline compared with more moderate coffee drinkers appeared to be explained by change in amount of coffee consumed during the long period of follow-up. When most recent, rather than baseline, coffee intake was considered, risk was higher in the heaviest drinkers (Table 4, column 3). Given the long follow-up and expected variation in coffee drinking over one’s lifetime, time-dependent analyses using most recent intake is the preferred approach.

The magnitude of the systolic blood pressor effect associated with drinking 1 cup of coffee (0.21 mm Hg) in this study was less than that seen in clinical trials of coffee drinking, but the effect for diastolic pressure (0.26 mm Hg) was almost identical. In a recent meta-analysis of 11 clinical trials lasting longer than 2 weeks (median duration, 56 weeks),3 the effect of drinking 1 cup a day was estimated to be 0.52 mm Hg for systolic pressure and 0.25 mm Hg for diastolic pressure.3 The blood pressure effects of drinking coffee are due to its caffeine content16 and adaptation to these effects occurs rapidly.17 Continued adaptation over the long period of follow-up in this study may explain why the effect on systolic pressure is less than that seen in clinical trials. In the Bus-
elston Study, the only prospective study of coffee drinking and blood pressure of which we are aware, persons who decreased their coffee intake experienced a fall in blood pressure over 6 years of follow-up.18 The risk of developing hypertension associated with coffee drinking has not been examined previously, to our knowl-
edge, but studies of the association of coffee drinking with risk of hemorrhagic stroke, a marker of uncontrolled hyper-
tension, have also not shown an association.19

In contrast to the relatively consistent results from clinical trials, cross-sectional studies where coffee in-
take and blood pressure were assessed at the same time have yielded mixed results.20-28 A problem with such studies is that persons with high blood pressure are often advised to moderate their coffee intake.27 Thus, inverse or J-shaped associations may result from selective de-
crease of coffee intake in those with elevated blood pres-
Sure. An advantage of the present study is that it is un-
likely that knowledge of high blood pressure affected level of coffee intake because first elevation of blood pressure was used to define time of onset of hypertension, often years before a clinical diagnosis was made and medica-
tion was started.

Method of coffee preparation has been shown to be an important determinant of the effects of coffee drinking on serum lipid levels because passing boiled coffee through a paper filter removes terpenes that raise serum cholesterol levels.29 Specific information about method of coffee preparation from the participants would be desirable but was unavailable. Calendar time, although sub-optimal, was used as a marker for method of coffee prepara-
tion in the present study because automatic drip coffee filters did not come into widespread use until after 1975. Thus, most of the coffee consumed prior to that time was probably percolated and unfiltered. Calendar time did not modify the association of coffee drinking with blood pressure or hypertension incidence, suggesting that method of coffee preparation does not affect hypertension risk.

Strengths of this study include the assessment of coffee intake prior to development of hypertension, very high response rates at baseline and follow-up, validity of self-reported blood pressure, and the repeated measures of coffee intake during a median follow-up of 33 years. The information on parental incidence of hypertension and the repeated measures of alcohol intake, physical activity, cigarette smoking, and body mass from an average age of 22 to 65 years, allowed adjustment for these possible confounding variables. Another unique strength is the ability to examine the effect of coffee drinking not only on risk of hypertension, but also on blood pressure. Utilization of GEE analysis allowed inferences of the impact of coffee drinking on blood pressure while taking into account changes in blood pressure due to age, intraindividual correlation in blood pressure over time, and the influence of other confounders.

The results presented herein are strictly generaliz-
able only to high socioeconomic status white men. The prevalence of hypertension in this cohort in 1995 was 28%, somewhat less than that for non–Hispanic white men aged 50 to 69 years in the United States as a whole.29 Information on other dietary factors associated with hyperten-
sion incidence, such as dietary intake of sodium, potas-
associated with higher levels of coffee intake. Relative risk estimates associated with coffee drinking were all less than 2.0 and, after adjustment for a number of factors associated with hypertension incidence, the risk associated with coffee drinking was no longer statistically significant.

The results presented herein are strictly generalizable only to high socioeconomic status white men. The prevalence of hypertension in this cohort in 1995 was 28%, somewhat less than that for non–Hispanic white men aged 50 to 69 years in the United States as a whole.

Table 4. Relative Risk of Hypertension Associated With Coffee Consumption in 1017 White Men During a Median Follow-up of 33 Years: Cox Proportional Hazards Analysis*

<table>
<thead>
<tr>
<th>Cups per Day</th>
<th>Baseline Intake</th>
<th>Most Recent Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted†</td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1-2</td>
<td>1.34 (0.95-1.90)</td>
<td>1.24 (0.87-1.77)</td>
</tr>
<tr>
<td>3-4</td>
<td>1.63 (1.12-2.38)</td>
<td>1.49 (1.01-2.20)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>1.35 (0.87-2.08)</td>
<td>1.07 (0.67-1.69)</td>
</tr>
<tr>
<td>P value for test of trend</td>
<td>.07</td>
<td>.49</td>
</tr>
</tbody>
</table>

*Data are given as relative risk (95% confidence interval).
†Models are stratified by year of graduation and adjusted for parental history of incident hypertension and time-dependent number of cigarettes smoked, alcohol intake, physical activity, and body mass index.
sium, and fiber, were not available. In a cross-sectional study of 1194 white men in the United States, however, coffee intake was not associated with dietary intake of bran fiber, fiber from fruit, or cruciferous vegetables.30 Cups of coffee per day were associated with levels of physical activity and alcohol intake, variables that were included in this analysis. More complete adjustment for the intensity and magnitude of possible confounders, however, may have entirely eliminated any association of coffee drinking with hypertension incidence. Because of the concern that the association of coffee drinking with hypertension risk may not be causal and that incidence rates of hypertension might not be generalizable, we did not calculate estimates of population attributable risk of hypertension associated with coffee intake.

Clinical trials conducted in persons with established hypertension have demonstrated that cessation of coffee drinking lowers blood pressure.31 Our results may not apply to such persons. In groups similar to our study population, however, coffee drinking does not appear to play a major role in the incidence of hypertension.

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