Coffee Consumption and the Risk of Coronary Heart Disease and Death

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Objectives: To study prospectively the relation of coffee drinking with fatal and nonfatal coronary heart disease (CHD) and all-cause mortality and to perform a cross-sectional analysis at baseline on the association between coffee drinking and CHD risk factors, diagnosed diseases, self-reported symptoms, and use of medicines.

Methods: The study cohort consisted of 20,179 randomly selected eastern Finnish men and women aged 30 to 59 years who participated in a cross-sectional risk factor survey in 1972, 1977, or 1982. Habitual coffee drinking, health behavior, major known CHD risk factors, and medical history were assessed at the baseline examination. Each subject was followed up for 10 years after the survey using the national hospital discharge and death registers. Multivariate analyses were performed by using the Cox proportional hazards model.

Results: In men, the risk of nonfatal myocardial infarction was not associated with coffee drinking. The age-adjusted association of coffee drinking was J shaped with CHD mortality and U shaped with all-cause mortality. The highest CHD mortality was found among those who did not drink coffee at all (multivariate adjusted). Also, in women, all-cause mortality decreased by increasing coffee drinking. The prevalence of smoking and the mean level of serum cholesterol increased with increasing coffee drinking. Non-coffee drinkers more often reported a history of various diseases and symptoms, and they also more frequently used several drugs compared with coffee drinkers.

Conclusions: Coffee drinking does not increase the risk of CHD or death. In men, slightly increased mortality from CHD and all causes in heavy coffee drinkers is largely explained by the effects of smoking and a high serum cholesterol level.

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Many published studies have found a positive association between coffee drinking and risk of coronary heart disease (CHD). Since the early 1970s, there has been good evidence that nonfiltered, boiled coffee increases the serum cholesterol level, especially the serum low-density lipoprotein cholesterol concentration, and thus increases the CHD risk. It appears that most of the cohort studies have not found any association, while many of the case-control studies have reported a positive association between coffee drinking and CHD. Some studies suggest that only heavy coffee drinking (>4-9 cups per day) increases the risk of CHD. Not all studies, however, support this hypothesis. Sometimes the strong association has weakened or disappeared after adjustment for major coronary risk factors or when the follow-up has been extended.

In Finland, the average coffee drinking per capita is one of the highest in the world. Also, CHD mortality is high among the Finnish population. In this study, we examined whether coffee drinking is associated with the risk of an acute coronary event, coronary death, and death from any causes, and whether the risk is independent of other CHD risk factors. In addition, we analyzed the association of coffee drinking with self-reported diseases, symptoms, and complaints and with the use of medicines. The amount of coffee consumed is given in cups, where 1 cup is equal to 1.1 dL. The mean caffeine content in 1 cup is 100 mg.

RESULTS

The changes in coffee drinking were small between 1972 and 1982. At each study year, the drinking of coffee per day was higher in men than in women. In men, the average amount of coffee consumed was...
SUBJECTS AND METHODS

STUDY POPULATION

Independent cross-sectional population surveys were carried out in 1972, 1977, and 1982 to assess the levels and trends of cardiovascular risk factors in the provinces of North Karelia and Kuopio in eastern Finland. In 1972 and 1977, a randomly selected sample of 6.6% of the population born between 1913 and 1947 was drawn in both areas. In 1982, the sample included people aged 25 to 64 years; the samples were stratified according to World Health Organization protocol (MONICA [monitoring trends and determinants in cardiovascular disease]) so that at least 250 subjects of each sex and each 10-year age group were chosen from both areas. In the present analyses, the 3 cohorts are combined. Those subjects who participated in more than one survey are included only in their first study cohort. The cohorts included a total of 12931 men and 12675 women. Those 10075 men (78%) and 10387 women (82%) who participated in the surveys and for whom we had complete data on smoking status, serum cholesterol level, blood pressure (BP), body mass index (BMI), and coffee drinking were included in this prospective analysis.

ASSESSMENT OF RISK FACTORS AND GENERAL HEALTH

The surveys included a self-administered questionnaire about dietary and drinking habits, health behavior, medical history, perceived health, use of medicines, and other health-related questions. The questionnaires were returned to the survey site, where specially trained nurses checked them to ensure that they were fully completed, measured BP and other variables, and took a venous blood specimen for the determination of serum cholesterol level.

Habitual coffee drinking was recorded as the number of cups consumed daily on the questionnaire (open question). The average number of cups of coffee consumed daily was 5.6 in men and 5.1 in women.

Smoking was assessed using a set of standardized questions on a self-administered questionnaire. The participants were classified into 3 categories: (1) current smokers—persons who had smoked regularly for at least 1 year and had smoked during the preceding month more than once a day on average, (2) ex-smokers, and (3) never smokers. In this study, never smokers and those ex-smokers who had not smoked for at least 6 months were considered to be nonsmokers, and those ex-smokers who had not smoked for less than 6 months were considered as smokers.

The serum cholesterol level was determined in 1972 and 1977 from frozen samples using the Burchard-Liebermann reaction (Auto Analyzer II-26a; Technicon Instruments Corp, Tarrytown, NY). In 1982, an enzymatic assay method was used (CHOD-PAP Monotest; Boehringer Mannheim, Mannheim, Germany). The enzymatic assay method gave 2.4% lower values than the Burchard-Liebermann method. The cholesterol values from 1972 and 1977 were corrected by this percentage. All cholesterol samples were analyzed in the same laboratory at the National Public Health Institute.

Blood pressure was measured from the right arm of the subject, who had been asked to sit for 5 minutes before the measurement. The fifth phase of the Korotkoff sounds was recorded as the diastolic BP. In 1972 and 1977, a shorter cuff (23 cm) was used than that used in 1982 (42 cm). Even though the BP measurements taken with the longer cuff may be slightly lower than the measurements taken with the shorter cuff, the change in cuff size does not affect the association between a 1-U change in BP and the end point (CHD and death) in the analyses. Further adjustment for study year had minor effect on the results (small changes in the second and third decimal in risk ratios).

Data on general health status included self-reported illnesses and symptoms, use of certain drugs (for cardiovascular disease, high BP, backache, skin diseases, cough, headache, and other aches; antacids and laxatives; contraceptives; sedatives; sleeping pills; and vitamin and mineral supplements), sick leave during the past year, and perceived health. The list of drugs on the questionnaire was the same in each survey.

ASCERTAINMENT OF END POINTS

Mortality data were obtained from the National Death Register at Statistics Finland. Data on nonfatal acute myocardial infarction (MI) were received from the National Hospital Discharge Register. Mortality data and National Hospital Discharge Register data were linked to the risk factor data using the national personal identification number assigned to every resident of Finland. The eighth revision of the Internal Classification of Diseases was used in Finland from 1969 to 1986. Nonfatal acute MI events, deaths from CHD, and deaths from any cause were used as separate end points. Acute coronary events were classified as follows: Internal Classification of Diseases codes 410 to 414 were classified as CHD deaths, and codes 410 to 411 in the National Hospital Discharge Register were classified as nonfatal MI. The follow-up of each subject included in our present analyses was 10 years, or until the end point occurred. The number of CHD events, either nonfatal or fatal, was 891 in men and 319 in women. The number of deaths from CHD and the total number of deaths were 509 and 1201 in men and 99 and 444 in women, respectively.

STATISTICAL ANALYSIS

Differences in the mean values of cardiovascular risk factors were tested using the analyses of variance. For proportions, a log-linear model was used as the statistical method. Multivariate analyses were performed by using the Cox proportional hazards model. The estimates of relative risks and their 95% confidence intervals were calculated based on this model. In the models, coffee drinking was used as a dummy variable at 4 drinking levels. A moderate drinking level, 1 to 3 cups of coffee daily, was used as the baseline level. The known cardiovascular risk factors, smoking status, serum cholesterol level, BP, and history of MI were included in the models. All analyses were adjusted for age. Statistical analyses were done using the SAS statistical program.
5.8, 5.4, and 5.7 cups per day in 1972, 1977, and 1982, respectively; in women, it was 5.4, 5.0, and 4.9 cups per day, respectively.

Subjects drinking 4 or more cups of coffee daily were older than those drinking less than 4 cups (Table 1). In men, the prevalence of smoking and the serum cholesterol level increased with increasing coffee drinking. Smoking was strongly associated with coffee drinking.

The systolic BP and BMI were slightly lower among non-drinkers than among coffee drinkers. The diastolic BP was slightly higher among light coffee drinkers (1-3 cups daily) than among nondrinkers, moderate coffee drinkers (4-7 cups daily), and heavy coffee drinkers (>7 cups daily).

In women, the serum cholesterol level and the prevalence of smoking increased with increasing coffee drinking, as in men (Table 1). Blood pressure tended to in-
crease also with increasing coffee drinking until 7 cups daily. The BMI had a J-shaped association with coffee drinking, being lowest in people with moderate coffee drinking and increasing thereafter with the increasing amount of coffee consumed.

In men, the risk of nonfatal MI was not associated with coffee drinking (Table 2). The age-adjusted risk ratio of CHD mortality showed a J-shaped association with coffee drinking, and that of total mortality was U shaped, being lowest in moderate coffee drinkers and higher in nondrinkers and in heavy coffee drinkers. When smoking status, serum cholesterol level, BP, and previous MI were added to the model, the risk ratios of CHD and total mortality were higher among nondrinkers compared with coffee drinkers.

In women, the risk ratio of nonfatal MI in nondrinkers was higher than in coffee drinkers in the multivariate model (Table 3). We found no significant association between coffee drinking and CHD mortality. The small number of these events prohibited full statistical analyses. Total mortality decreased with increasing coffee drinking, and it was significantly ($P = .07$, multivar-
iterative model) lower among heavy coffee drinkers than among nondrinkers or light or moderate coffee drinkers.

Men who drank less than 1 cup of coffee daily more often reported back illnesses, constipation, nausea, night-mares, sleeplessness, and headache compared with men who drank 1 cup or more of coffee daily (Table 4 and Table 5). Heavy coffee drinking was inversely associated with self-reported heart failure and gallstones or cholecystitis. Nondrinkers and light coffee drinkers more often reported dry mouth and a stuffed up nose than moderate or heavy coffee drinkers. Light and moderate coffee drinkers more often reported high BP than nondrinkers and heavy coffee drinkers. The amount of coffee drinking and the self-reported prevalence of exhaustion and overstrain had a U-shaped association. Men who drank less than 1 cup of coffee daily more often reported using antacids or laxatives compared with others (Table 6). After a further adjustment for CHD risk factors (smoking, high serum cholesterol level, high BP, and previous MI), most of these differences still existed (results from multivariate analysis are not shown in the tables).

Women who drank less than 1 cup of coffee daily more often reported angina pectoris, emphysema or chronic bronchitis, constipation, and repeated stomachaches than coffee-drinking women (Tables 4 and 5). Nondrinkers and light coffee drinkers more often reported heart failure, gallstones or cholecystitis, nausea, dry mouth, and stuffed up nose than women who drank 4 or more cups of coffee daily. Light and moderate coffee drinkers more often reported high BP than nondrinkers or heavy coffee drinkers. Coffee drinking showed a U-shaped association with the self-reported prevalence score of joint ache and stress or nervousness. Women who drank less than 1 cup of coffee daily more often reported using sedatives, sleeping pills, and antacids or laxatives compared with others (Table 6). The adjustment for confounding factors had virtually no effect on these results.

The prevalence of smoking was significantly (P<.001) higher among men than among women.

<table>
<thead>
<tr>
<th>Table 5. Prevalence of Some Self-Reported Symptoms and Complaints During the Previous Month by Coffee Consumption*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms and Complaints</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Joint ache</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Repeated stomach aches</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Dry mouth</td>
</tr>
<tr>
<td>Stuffed up nose</td>
</tr>
<tr>
<td>Excited heartbeat</td>
</tr>
<tr>
<td>Trembling in the hands</td>
</tr>
<tr>
<td>Stress or nervousness</td>
</tr>
<tr>
<td>Frightening thoughts</td>
</tr>
<tr>
<td>Exhaustion and overstrain</td>
</tr>
<tr>
<td>Dizziness</td>
</tr>
<tr>
<td>Nightmares</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Sleeplessness</td>
</tr>
<tr>
<td>Headache</td>
</tr>
</tbody>
</table>

*Data are given as percentage of men and women.
†The amount of coffee consumed is given in cups per day, where 1 cup is 1.1 dL. The mean caffeine content in 1 cup is 100 mg.
‡Adjusted for age and study year.
levels of serum cholesterol and BP were also higher among men. Men more often reported angina pectoris, emphysema or chronic bronchitis, back illness, and stuffed up nose than women (data not shown).

The BMI was higher among women than among men. Women more often reported high BP, gallstones or cholecystitis, joint ache, constipation, nausea, and excited heartbeat than men.

**Comment**

We found no association between coffee drinking and the risk of nonfatal MI. Coronary heart disease mortality was highest among non–coffee drinkers. In men, the association between coffee drinking and total mortality was U shaped (ie, the lowest mortality in men was in those who drank a moderate amount of coffee), while in women, total mortality decreased with increasing coffee drinking. Thus, our findings do not support the hypothesis that heavy coffee drinking is a risk factor for CHD.

During the past 20 years, several epidemiological and experimental studies in different countries have reported on the effects of coffee on the CHD risk. Most of the published cohort studies have not found a positive association between coffee drinking and CHD, while many case-control studies have reported a positive association. Some case-control studies have been criticized because of poor control for confounding, selection bias, or recall bias. One suggested explanation for the discrepancy between the findings from cohort and case-control studies is that coffee might act as a triggering event in people with chronic CHD, leading to an MI, rather than as a causal and biological risk factor for CHD. Coffee drinking itself has probably mainly short-term effects on the CHD risk, which the cohort studies would obviously miss.

It has been suggested that the dose-response relation between coffee drinking and the risk of CHD may be more complex than previously recognized. Some studies have been criticized for not fully studying the dose-response relation because of lack of sufficient data in the higher coffee-drinking categories. This is a common problem in several studies in countries where coffee drinking is not particularly high. In most studies, the measurement of coffee use has been relatively crude. The drinking has usually been recorded in cups per day, without taking into account the effect of varying cup sizes. In Finland, coffee drinking is a social habit, and it is common to drink coffee everywhere. The size of a coffee cup in Finland does not vary much. The average size of the standard cup was 1.1 dL in the 1970s. The mean caffeine content of one Finnish cup of coffee is 100 mg. One standard cup of espresso coffee (0.35 dL) also contains 100 mg of caffeine. Finland has one of the highest consumption of coffee per capita (13.0 kg) in the world. In our study, approximately 78% of the participants drank 4 or more cups of coffee daily. Thus, we had sufficient power to study the dose response, although in women the number of CHD deaths was small.

Unfiltered, boiled coffee has been shown to elevate the serum cholesterol level, especially the level of low-density lipoprotein cholesterol. The effect of coffee preparation method may partly explain the conflicting results of the previous cross-sectional studies on coffee consumption and cholesterol level. The strongest positive associations between coffee drinking and the serum cholesterol concentration have been reported from the Nordic countries, where boiled coffee has been commonly used until recently. Our results supported the hypothesis that coffee consumption elevates the serum cholesterol level, because the serum cholesterol level increased with increasing coffee drinking. Unfortunately, we did not have detailed data on the method of preparation of coffee in our surveys, but at the end of the 1960s, the proportion of the users of boiled coffee was 75%. In 1987, 24% of Finns drank boiled and 69% drank filtered coffee. It has been shown that boiled coffee contains a lipid-rich fraction that powerfully elevates the levels of serum total and low-density lipoprotein cholesterol. The most

**Table 6. Prevalence of Self-Reported Use of Some Medicines During the Previous Year by Coffee Consumption**

<table>
<thead>
<tr>
<th>Use of Medicines</th>
<th>&lt;1</th>
<th>1-3</th>
<th>4-7</th>
<th>&gt;7</th>
<th>P†‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong> (n = 599)</td>
<td>(n = 1808)</td>
<td>(n = 5640)</td>
<td>(n = 2719)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For headache</td>
<td>21.0</td>
<td>19.3</td>
<td>20.8</td>
<td>21.7</td>
<td>.36</td>
</tr>
<tr>
<td>For other aches</td>
<td>22.5</td>
<td>18.6</td>
<td>21.7</td>
<td>23.3</td>
<td>.02</td>
</tr>
<tr>
<td>Sedatives</td>
<td>10.5</td>
<td>8.0</td>
<td>6.9</td>
<td>8.2</td>
<td>.14</td>
</tr>
<tr>
<td>Sleeping pills</td>
<td>10.7</td>
<td>8.0</td>
<td>7.2</td>
<td>8.3</td>
<td>.14</td>
</tr>
<tr>
<td>Antacids and laxatives</td>
<td>20.7</td>
<td>10.3</td>
<td>8.0</td>
<td>5.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Women</strong> (n = 391)</td>
<td>(n = 1896)</td>
<td>(n = 7144)</td>
<td>(n = 1594)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For headache</td>
<td>33.5</td>
<td>32.5</td>
<td>32.6</td>
<td>36.9</td>
<td>.12</td>
</tr>
<tr>
<td>For other aches</td>
<td>30.4</td>
<td>24.9</td>
<td>25.1</td>
<td>29.6</td>
<td>.77</td>
</tr>
<tr>
<td>Sedatives</td>
<td>14.4</td>
<td>11.3</td>
<td>10.1</td>
<td>10.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sleeping pills</td>
<td>14.4</td>
<td>11.9</td>
<td>10.2</td>
<td>10.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antacids and laxatives</td>
<td>19.2</td>
<td>11.5</td>
<td>7.3</td>
<td>7.3</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

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‡Adjusted for age and study year.
likely cholesterol-raising compounds in boiled coffee are cafestol and possibly kahweol. Cafestol and kahweol are naturally occurring substances in coffee beans. It is proposed that bile acid production and secretion could have something to do with this association. In the mid-1980s, it was found that coffee may contain more than 100 active chemicals, depending on the brewing method. The mechanism by which these substances operate is not known, but it has been suggested that altered liver functions are associated with coffee drinking. It has been suggested that coffee might have other effects on cardiovascular risk. For example, in a Norwegian study, coffee was shown to be a strong predictor for coronary death even beyond what could be explained by the cholesterol-raising effects.

Several epidemiological studies7,20,29-32 have demonstrated that smokers usually drink more coffee and have a lower level of physical activity than nonsmokers, which are explained to be a result of clustering of unhealthy lifestyle habits in certain individuals. We found positive associations between heavy coffee drinking and a high prevalence of smoking and a high serum cholesterol level in both sexes, and a high BMI in women.

A descriptive analysis of our data revealed that noncoffee-drinking subjects had a higher prevalence of several self-reported diseases and symptoms than coffee drinkers. It is probable that many nondrinkers had stopped coffee drinking because of their underlying diseases or symptoms. We did not ask about history of coffee drinking in our surveys and, therefore, cannot answer this question. Several diseases and symptoms showed a U-shaped association with coffee drinking. However, heavy coffee drinking, which is associated with a higher prevalence of some diseases and symptoms compared with light and moderate drinking, did not increase the risk for CHD in women. There is evidence that a low risk associated with drinking up to 4 cups of coffee per day can also reflect a protective effect of light or moderate coffee drinking, because coffee contains chlorogenic and caffeic acids that may have antioxidant properties. In addition, it is possible that heavy coffee drinkers have developed tolerance to the neurohumoral effects of caffeine.

Results concerning the association of coffee and BP in previous epidemiological studies are complicated. Of 12 studies in which BP was measured, 4 expressed no association, 4 had a positive association, and 4 had an inverse association. One potential explanation for these inconsistencies is that epidemiological studies have sometimes failed to take into account study subjects’ systematic caffeine concentrations at the time when BP was measured, as the potential effect of coffee on BP is likely to be short-term. It has been shown that caffeine can increase short-lived BP in the order of 10%. Although it appears that coffee increases BP in the short-term, participants might have avoided coffee before BP measurement, and the hypotensive effects of caffeine abstinence still persisted. In our study, the participants were advised to abstain from coffee overnight. Nevertheless, in women, the BP increased with increasing coffee consumption up to 7 cups daily.

There are reports of caffeine-induced improvements on motor and psychomotor mechanisms, but also studies of caffeine having no effect on such tasks. Caffeine possibly influences a human’s physiological response to hypoglycemia. If caffeine intake increase the subject’s sensitivity and the awareness of hypoglycemia, caffeine may be a useful therapy for people with diabetes. On the other hand, caffeine may alert people to also recognize other types of symptoms. Thus, heavy coffee drinkers may report more symptoms than nondrinkers.

Since coffee is a commonly consumed drink, the association between coffee drinking and various diseases has been studied previously. Several studies have documented caffeine withdrawal symptoms in habitual coffee drinkers. Unfortunately, in this cross-sectional assessment of the baseline risks, we did not have data on ex-coffee drinkers. Caffeine withdrawal has been reported itself as headache, disrupted motor performance, depression, and other symptoms lasting up to 1 week, and has been reported to occur in persons who consume low to moderate amounts of caffeine. In our study, an increase in coffee drinking was related to a decreasing tendency of self-reported heart failure, gallstones or cholecystitis, constipation, and repeated stomachaches. In men, the prevalence of self-reported angina pectoris was similar over the categories of coffee drinking, but in women angina pectoris was common among nondrinkers. Our findings of the associations of coffee drinking and self-reported heart failure and angina pectoris confirmed our main results concerning coffee drinking and the increased risk for CHD among nondrinkers. Also, our results are in keeping with a recent report suggesting that coffee drinking may be protective against gallstones.

The increased risk of CHD mortality and also of total mortality among those not drinking coffee is an interesting finding. A potential explanation is that these subjects really had underlying diseases and thus the higher risk. It is probable that there were many other reasons that might have lead to a reduction in coffee drinking. Even though avoiding coffee has become somewhat more common among young people in Finland, it was unusual for a middle-aged Finn not to drink coffee in the 1970s and 1980s. Usually people gave up coffee only because of some health reasons. In conclusion, our results provide further evidence that coffee drinking does not increase the risk of nonfatal MI in this high-risk Finnish population. In men, the slightly increased risk of CHD and total mortality in heavy coffee drinkers is largely explained by the effects of smoking and high serum cholesterol level.

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