Coffee Consumption and Risk of Stroke in Women

Susanna C. Larsson, PhD; Jarmo Virtamo, MD; Alicja Wolk, DMSc

Background and Purpose—Coffee consumption has been inconsistently associated with stroke incidence and mortality in previous studies. We investigated the association between coffee consumption and stroke incidence in the Swedish Mammography Cohort.

Methods—We prospectively followed 34,670 women without a history of cardiovascular disease or cancer at baseline in 1997. Coffee consumption was assessed in 1997 using a self-administered questionnaire. Incident stroke cases were ascertained from the Swedish Hospital Discharge Registry.

Results—During a mean follow-up of 10.4 years, we ascertained 1680 stroke events, including 1310 cerebral infarctions, 154 intracerebral hemorrhages, 79 subarachnoid hemorrhages, and 137 unspecified strokes. After adjustment for other risk factors, coffee consumption was associated with a statistically significant lower risk of total stroke, cerebral infarction, and subarachnoid hemorrhage but not intracerebral hemorrhage. The multivariable relative risks of total stroke across categories of coffee consumption (<1 cup/day, 1 to 2 cups/day, 3 to 4 cups/day, and ≥5 cups/day) were 1.00, 0.78 (95% CI, 0.66 to 0.91), 0.75 (95% CI, 0.64 to 0.88), and 0.77 (95% CI, 0.63 to 0.92, respectively; P for trend = 0.02). The association between coffee consumption and cerebral infarction was not modified by smoking status, body mass index, history of diabetes or hypertension, or alcohol consumption.

Conclusions—These findings suggest that low or no coffee consumption is associated with an increased risk of stroke in women. (Stroke. 2011;42:911-915.)

Key Words: coffee ■ epidemiology ■ prospective studies ■ stroke ■ women
3 SDs from the log-transformed mean energy intake). This left 34,670 women aged 49 to 83 years for the analysis. The study was approved by the Ethical Review Board at the Karolinska Institutet (Stockholm, Sweden).

### Baseline Data Collection

The 1997 questionnaire included questions on education, weight, height, cigarette smoking, physical activity, aspirin use, history of diabetes and hypertension, family history of myocardial infarction before 60 years of age, alcohol consumption, and diet. Body mass index was calculated by dividing the weight in kilograms by the square of height in meters. Pack-years of smoking history were calculated as the number of packs of cigarettes smoked per day multiplied by the number of years of smoking. The participants reported their level of activity at work, home/housework, walking/bicycling, and exercise in the year before study enrollment. The questionnaire also included questions on inactivity (watching TV/reading) and hours per day of sleeping and sitting/lying down. The reported time per day reported by the subject to have engaged in each activity was multiplied by the activity’s typical energy expenditure requirement expressed in metabolic equivalents. The metabolic equivalent-hours for all of the individual activities reported by the subject were then added together to create a metabolic equivalent-hours per day (24-hour) score.16

### Assessment of Coffee Consumption

Coffee consumption was assessed using a self-administered food-frequency questionnaire that included 96 foods and beverages. For coffee, participants were asked to indicate how many cups of coffee per day or per week they consumed during the past year. The questionnaire did not inquire about the type of coffee consumed (eg, regular or decaffeinated coffee) because consumption of decaffeinated coffee in the Swedish population is very low. In our validation study, the Pearson correlation coefficient between the food-frequency questionnaire and the mean of 4 1-week diet records was 0.6 for coffee (A. Wolk, unpublished data).

### Case Ascertainment and Follow-Up

Incident cases of first stroke that occurred between January 1, 1998, and December 31, 2008, were ascertained by linkage of the study cohort with the Swedish Hospital Discharge Registry, which provides almost complete coverage of the discharges. The International Classification of Diseases, 10th Revision, was used to identify stroke events. The stroke events were classified as cerebral infarction (International Classification of Diseases, 10th Revision, code I63), intracerebral hemorrhage (I61), subarachnoid hemorrhage (I60), and unspecified stroke (I64). Information on dates of death was obtained from the Swedish Cause of Death Registry.

### Statistical Analysis

Person-time of follow-up for each participant was calculated from January 1, 1998, to the date of the first stroke event, death, or end of follow-up (December 31, 2008), whichever occurred first. We used Cox proportional hazard models with age as the time scale to estimate the relative risks (RRs) with 95% CIs of stroke by categories of coffee consumption. Entry time was defined as a subject’s age in months at start of follow-up, and exit time was defined as a subject’s age in months at stroke diagnosis, death, or end of follow-up. The proportional hazards assumption was tested and found to be satisfied for all variables except diabetes. We adjusted for diabetes by stratification in the Cox model. The multivariable model included the following variables: smoking status and pack-years of smoking (never; past <20, 20 to 39, or ≥40 pack-years; or current <20, 20 to 39, or ≥40 pack-years); education (less than high school, high school, or university); body mass index (<20, 20 to 24.9, 25 to 29.9, or ≥30 kg/m2); total physical activity (metabolic equivalent hours/day, quartiles); self-reported history of hypertension (yes or no); aspirin use (yes or no); family history of myocardial infarction before 60 years of age (yes or no); intakes of total energy (kcal/day, continuous variable) and alcohol (non-drinkers or <3.4, 3.4 to 9.9, or ≥10.0 g/day); and quartiles of red meat, fish, fruits, and vegetables. Tests for trends across categories were conducted by modeling coffee consumption as a continuous variable using the median value of each category of coffee.

We conducted stratified analyses to assess whether the association of coffee consumption with stroke risk was modified by smoking status (never/past or current), body mass index (<30 or ≥30 kg/m2), diabetes (yes or no), hypertension (yes or no), and alcohol consumption (abstainer or drinker). To test the statistical significance of interactions on a multiplicative scale, we used the log likelihood ratio test comparing the models with or without interaction terms. All statistical analyses were performed using SAS Version 9.1 (SAS Institute Inc, Cary, NC). All probability values were 2-sided.

### Results

During a mean follow-up of 10.4 years, we ascertained 1680 stroke events, including 1310 cerebral infarctions, 154 intracerebral hemorrhages, 79 subarachnoid hemorrhages, and 137 unspecified strokes. The baseline characteristics of the study cohort by categories of coffee consumption are presented in Table 1. The median daily coffee consumption was 3 cups (interquartile range, 2 to 4 cups). Compared with women with a low coffee consumption, those with a high consumption were less likely to have a university education and more likely to be smokers. They also were somewhat less likely to have a history of diabetes or hypertension and consumed less fruits and vegetables.

The risk of total stroke was statistically significantly associated with smoking (current versus never smoking, multivariable RR, 1.38; 95% CI, 1.22 to 1.57), education (university versus primary school, multivariable RR, 0.74; 95% CI, 0.61 to 0.89), and history of hypertension (multivari-
Obesity was associated with an increased risk of cerebral infarction (BMI 30 kg/m² versus 20 to 24.9 kg/m², multivariable RR, 1.28; 95% CI, 1.07 to 1.52), and a family history of coronary heart disease was positively associated with risk of intracerebral hemorrhage (multivariable RR, 1.61; 95% CI, 1.06 to 2.45). Aspirin use and total physical activity were not statistically significantly associated with total stroke or any stroke subtype.

Aspirin use and total physical activity were not statistically significantly associated with total stroke or any stroke subtype. The association between coffee consumption and risk of total stroke and stroke subtypes is shown in Table 2. There was no statistically significant association between consumption of coffee and risk of stroke in the age-adjusted analysis. However, after adjustment for smoking (main confounder) and other risk factors, women who consumed 1 to 2 cups, 3 to 4 cups, or >5 cups of coffee per day had a statistically significant 22% to 25% lower risk of stroke compared with those who drank <1 cup of coffee per day. Coffee consumption was associated with decreased risk of cerebral infarction and subarachnoid hemorrhage but not intracerebral hemorrhage. When we compared women who consumed ≥1 cups of coffee per day with those who consumed <1 cup per day, the multivariable RR of total stroke was 0.76 (95% CI, 0.66 to 0.88). The association between coffee consumption and risk of total stroke did not vary statistically significantly by smoking status, body mass index, history of diabetes or hypertension, or alcohol consumption (Table 3).

### Discussion
In this population-based cohort of Swedish women, women who consumed ≥1 cups of coffee daily had a lower risk of stroke compared with women who consumed <1 cup of coffee daily. There was no dose–response relationship between coffee consumption and risk of total stroke; rather, the risk appeared to be increased among women with low or no consumption of coffee. An inverse association between coffee consumption and stroke was observed for cerebral infarction and subarachnoid hemorrhage but not intracerebral hemorrhage. The association was not modified by smoking status, body mass index, history of diabetes or hypertension, or alcohol consumption.
reduce the risk of stroke include attenuation of subclinical
inflammation, reduction in oxidative stress, and improved insulin sensitivity. A recent clinical trial showed that high consumption of filtered coffee (=8 cups/day) versus no consumption led to a significant decrease in serum concentrations of interleukin-18 and 8-isoprostane and a significant increase in adiponectin, total cholesterol, high-density lipoprotein cholesterol, and apolipoprotein A-I concentrations. Moreover, an observational study among women found that caffeinated coffee consumption was inversely associated with plasma concentrations of E-selectin (surface leukocyte adhesion molecules) and C-reactive protein (a marker of chronic low-grade inflammation) in diabetic women and that decaffeinated coffee consumption was inversely associated with C-reactive protein concentrations in healthy women. An inverse association between coffee consumption and C-reactive protein concentrations has also been observed in Japanese populations. In addition, habitual coffee consumption has been associated with higher insulin sensitivity.

Strengths of this study include its prospective and population-based design and the almost complete follow-up of study participants by linkage with population-based Swedish registers. A limitation of this study is that coffee consumption was assessed using a self-administered questionnaire, which will inevitably lead to some measurement error and misclassification of exposure. Another limitation is that our assessment of medical history and other covariates was based on self-report, which is less reliable than clinical measurements. Furthermore, although we adjusted for major risk factors for stroke, we cannot rule out the possibility that our findings may be due to unmeasured or residual confounding. There was no dose–response relation between coffee consumption and risk of cerebral infarction; rather, the risk
seemed to be increased among women who consumed <1 cup of coffee per day. We cannot entirely exclude the possibility that women with low coffee consumption may be more likely to be exposed to another unknown risk factor for stroke. However, the association persisted after adjustment for other known stroke risk factors.

In summary, in this prospective study of Swedish women, low or no coffee consumption was associated with an increased risk of stroke. Additional prospective studies on coffee consumption and stroke incidence as well as mechanistic studies investigating possible effects of coffee consumption on cardiovascular risk factors are warranted.

Sources of Funding
This study was supported by research grant from the Swedish Council for Working Life and Social Research (FAS) and the Swedish Research Council for Infrastructure.

Disclosures
None.

References
Coffee Consumption and Risk of Stroke in Women
Susanna C. Larsson, Jarmo Virtamo and Alicja Wolk

Stroke. published online March 10, 2011;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/early/2011/03/10/STROKEAHA.110.603787

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2012/03/12/STROKEAHA.110.603787.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/
여성에서의 커피 섭취와 뇌졸중 위험도

Coffee Consumption and Risk of Stroke in Women

Susanna C. Larsson, PhD; Jarmo Virtamo, MD; Alicja Wolk, DMSc

(Stroke. 2011;42:908-912.)

Key Words: coffee ■ epidemiology ■ prospective studies ■ stroke ■ women

배경과 목적
이전 연구들에서 커피 섭취는 뇌졸중 발생 및 사망과 관련된 연관성을 보여 주지 않았다. 저자들은 Swedish Mammography Cohort에서 커피 섭취와 뇌졸중 발생의 연관성을 위하여 조사하였다.

방법
저자들은 1997년 당시 심혈관질환이나 암 병력이 없는 여성 34,670명을 전향적으로 추적 조사하였다. 커피 섭취는 1997년에 스스로 작성한 설문지를 통하여 평가하였다. 뇌졸중의 발생은 Swedish Hospital Discharge Registry에서 확인하였다.

결과
10.4년의 평균 추적 조사 기간 동안 1,680건의 뇌졸중이 확인되었으며, 그 중 1,310건은 뇌경색(cerebral infarction), 154건은 뇌내출혈(intracerebral hemorrhage), 79건은 거미막하출혈(subarachnoid hemorrhage), 137건은 명시되지 않은 뇌졸중이었다. 다른 위험인자를 보정한 후 커피 섭취는 통계적으로 유의하게 전체 뇌졸중, 뇌경색, 거미막하출혈의 위험도는 낮추었으나 뇌내출혈의 위험도를 낮추지 않았다. 커피 섭취량(하루 1컵 비만, 하루 1~2컵, 하루 3~4컵, 하루 5컵 이상)에 따른 전체 뇌졸중의 다변수 상대위험도는 각각 1.00, 0.78 (95% CI, 0.66~0.91), 0.75 (95% CI, 0.64~0.88), 0.77 (95% CI, 0.63~0.92; P for trend=0.02)이었다. 커피 섭취와 뇌경색의 연관성은 흡연 상태, 체질량지수, 당뇨병이나 고혈압 병력, 알코올 섭취에 의하여 변경되지 않았다.

결론
이러한 소견은 커피를 적게 섭취하거나 섭취하지 않는 것이 여성에서 뇌졸중의 위험도를 높인다는 것을 시사한다.