# Inverse Relationship between Coffee Consumption and Cerebral Microbleeds in Men, but Not Women

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*Background:* Studies evaluating the association between coffee consumption and neurovascular diseases have frequently yielded contradictory results. The aim of this study was to investigate the association of coffee consumption with small-vessel disease (SVD) incidence in a healthy urban population while accounting for multiple demographic and lifestyle risk factors. *Methods:* This prospective study conducted from May 2013 through March 2014 included 455 participants (314 men and 141 women) aged 25 to 92 years. All subjects completed a questionnaire on coffee consumption and received a comprehensive neurologic examination, including magnetic resonance imaging, at St. Luke's International Hospital (Tokyo, Japan). *Results:* Incidence of SVD was lower in male daily coffee drinkers than male nondrinkers and occasional drinkers, whereas incidence of white matter lesions was lower in female daily coffee drinkers than female nondrinkers or occasional drinkers. In multivariate analyses including age, sex, smoking status, and BMI, as well as coffee consumption, incidence of microbleeds was significantly lower in male daily coffee drinkers compared to nondrinkers. *Conclusions:* Daily coffee consumption is associated with reduced risk of cerebral microbleeds in men. **Key Words:** Coffee consumption—microbleeds—small-vessel disease—beverage.


Numerous studies have investigated the relationships between daily beverage consumption and lifestyle diseases such as stroke. For example, greater consumption of sugar-sweetened soda by women has been associated with ischemic stroke, and consumption of low-calorie soda by women has been associated with hemorrhagic stroke.[1] Regular coffee consumption has been reported to increase mortality risk of lifestyle diseases, but reverse associations between coffee consumption and disease-specific mortality rates were found in the recent large-scale National Institutes of Health-AARP Diet and Health Study, including lower death rates due to heart disease, respiratory disease, and stroke (intracerebral hemorrhage, subarachnoid hemorrhage, and cerebral infarction) in regular consumers.[2] Moreover, 4 to 5 cups per day was inversely associated with apoplexic death in both men and women.[2] Conversely, several studies reported that coffee consumption increases the risk of aneurysmal subarachnoid hemorrhage,[3,4] but these studies also acknowledged a possible confound of cigarette smoking. Thus, there is no consensus on the risks of lifestyle diseases associated with coffee consumption alone.

Small-vessel disease (SVD) is a new category of central nervous system vascular disease that includes

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The authors declare that they have nothing to disclose.

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microbleeds, asymptomatic cerebral infarction, and white matter lesions. It is associated with arteriosclerosis in the central nervous system and with progressive microinfarcts and concomitant cognitive decline. This study examined the association between SVD and coffee consumption in healthy men and women scheduled for neurologic examinations at St. Luke's International Hospital, Tokyo, Japan, using univariate and multivariate analyses.

## Materials and Methods

This study was approved by St Luke's International Hospital Clinical Research Committee, and all participants gave their informed consent before participating. Healthy adults scheduled for neurologic examinations between May 2013 and March 2014 were given a questionnaire on admission about their coffee-drinking habits, including average number of cups consumed daily during the previous year and type(s) of coffee (eg, roasted, instant, or canned).

Multivariate analysis included the following lifestyle factors obtained from electronic medical records: smoking (current smoker versus never and past smoker), alcohol consumption (>30 g/day), and body mass index. Brain magnetic resonance imaging was performed using a 1.5-T Intera system (Philips, New York, NY) with axial T2*-weighted gradient echo and T2-weighted fluid-attenuated inversion recovery.

## Statistical Analyses

All statistical analyses were performed using SPSS (version 21; IBM, Tokyo, Japan) or JMP (version 11; SAS Institute Japan Ltd., Tokyo, Japan). Variables are expressed as mean ± standard deviation or number of patients (%) as appropriate. The chi-square test or Fisher exact test was performed to assess group differences in categorical variables. Receiver operating characteristic (ROC) curves were evaluated by univariate analysis. Multivariate logistic regression analysis was performed to identify independent factors associated with SVD.

## Coffee Cup-Years

The coffee cup-year is a unit for measuring the amount of coffee a person has drunk over a long period of time. It is calculated by multiplying the number of cups of coffee drunk per day by the number of years the person has drunk coffee.

$$\text{Coffee cup} - \text{years} = (\text{number of cups of coffee per day}) \times (\text{number of years drunk})$$

**Table 1.** *Patient clinicodemographic data and questionnaire results*

| Gender | Male | Female | Total |
|---|---|---|---|
| Number | 314 | 141 | 455 |
| Age (y), mean (SD) | 62.8 (12.5) | 64.5 (11.6) | 63.3 (12.2) |
| Drinking pattern | | | |
| DD | 179 | 78 | 257 |
| OD | 73 | 27 | 100 |
| ND | 62 | 36 | 98 |
| Roasted | 209 | 82 | 291 |
| Instant | 26 | 16 | 42 |
| Canned | 17 | 7 | 24 |
| Microbleeds | 36 (11.5) | 16 (11.3) | 52 (11.4) |
| Asymptomatic infarction | 37 (11.8) | 14 (9.9) | 51 (11.2) |
| White matter lesion | 119 (37.9) | 58 (41.1) | 177 (38.9) |

Abbreviations: DD, daily coffee drinker; ND, non–coffee drinker; OD, occasional drinker; SD, standard deviation.
Findings are presented as number (percentage).

## Results

During the study period, 455 of 515 participants scheduled for neurologic examination (314 men and 141 women) at St. Luke's International Hospital completed the coffee consumption questionnaire (88%). Findings are presented in Table 1. There were no significant differences in demographic variables, distribution of coffee-drinking habits (non-, occasion, and daily), or total SVD incidence based on sex.

Male daily coffee consumers exhibited a significantly lower incidence of SVD (all 3 forms), whereas female daily coffee drinkers showed a lower incidence of asymptomatic infarction (Table 2). Results were similar comparing nondrinkers to occasional and daily drinkers (data not shown).

In multivariate analysis including sex, age, alcohol consumption, current smoking status, body mass index, and coffee-drinking habits, incidence of microbleeds was significantly lower in male daily coffee drinkers than male non–coffee drinkers (Table 3). Moreover, male daily coffee drinkers also had significantly lower incidence compared to occasional drinkers (data not shown). We examined disease incidence according to duration of coffee consumption. There was a significant negative correlation between the number of coffee cup-years and microbleeds in men according to ROC curve analysis