Tea Consumption and Ischemic Stroke Risk
A Case–Control Study in Southern China

Wenbin Liang, MPH; Andy H. Lee, PhD; Colin W. Binns, MBBS, PhD; Rongsheng Huang, MBBS; Delong Hu, MD; Qingkun Zhou, MD

Background and Purpose—Although experimental studies have suggested that tea consumption may reduce the risk of ischemic stroke, available epidemiological evidence is equivocal, mainly due to the lack of accurate measurements on tea exposure. This study aims to ascertain the relationship between tea drinking and ischemic stroke risk.

Methods—A case–control study was conducted in southern China from 2007 to 2008. A total of 374 patients with incident ischemic stroke and 464 control subjects (mean age, 69 years) were recruited from 3 hospitals in Foshan. Information on frequency and duration of tea drinking, quantity of dried tea leaves, and types of tea consumed, together with habitual diet and lifestyle characteristics, was obtained from participants using a validated and reliable questionnaire. Logistic regression analyses were performed for tea consumption variables accounting for confounders that affect the ischemic stroke risk.

Results—A significant decrease in ischemic stroke risk was observed for drinking at least one cup of tea weekly ($P=0.015$) when compared with infrequent or nondrinkers, the risk reduction being largest by drinking one to 2 cups of green or oolong tea daily. Significant inverse dose–response relationships were also found for years of drinking and the amount of dried tea leaves brewed. The adjusted ORs for the highest level of consumption in terms of frequency of intake, duration of drinking, and average tea leaves brewed were 0.61 (95% CI, 0.40 to 0.94), 0.40 (95% CI, 0.25 to 0.64), and 0.27 (95% CI, 0.16 to 0.46), respectively.

Conclusion—Long-term tea consumption is associated with reduced risk of ischemic stroke. (Stroke. 2009;40:2480-2485.)

Key Words: case–control study ■ epidemiology ■ green tea ■ prevention ■ stroke risk

It is estimated that worldwide, 5 million people die from stroke annually accounting for approximately 10% of the total deaths.1 Ischemic stroke contributes >70% of all stroke cases in Western countries and approximately 60% in China and Japan.2–5 Experimental studies have suggested that tea drinking may prevent ischemic stroke. Although the underlying biological mechanisms are not completely understood and discrepancies exist, the literature has suggested that tea or its components could reduce hypertension, atherosclerosis, and thrombogenesis, which in turn are important risk factors for stroke.6 On the other hand, epidemiological evidence is still emerging and quite limited. An extensive literature search located 6 human observational studies investigating tea consumption and stroke risk (either ischemic or stroke type unspecified),7–12 but their results have been inconsistent. Fatal stroke rather than incident stroke was typically adopted as the outcome of interest,8–11 yet reported case-fatality rates varied between 15% and 57%, probably due to differences in acute stroke management and quality of care provided.13 Hemorrhagic strokes are also known to have a higher fatality rate than ischemic strokes.1,14 Therefore, the apparent association between tea consumption and stroke may be confounded by the disparity in medical treatment for acute stroke and the large proportion of fatal hemorrhagic stroke cases. Furthermore, long-term tea consumption was not assessed in these published studies. The onset of ischemic stroke is often based on the final stage of atherosclerosis, which requires many years to develop, whereas tea consumption has been shown to protect against the formation of atherosclerosis.6 Information on long-term tea exposure is thus important. Taking these issues into consideration, the present case–control study aims to ascertain the relationship between tea drinking and ischemic stroke risk.

Methods

Study Design and Eligibility Criteria
A hospital-based case–control study was conducted in the Guandong Province of southern China between July 2007 and July 2008. Subjects were recruited from 3 teaching hospitals within Foshan city, namely, the First People’s Hospital of Shunde, First People’s...
Hospital of Nanhui, and Second People’s Hospital of Foshan. Cases were patients with incident ischemic stroke referred from neurology departments’ inpatient wards, whereas control subjects were recruited from outpatient clinics of the Departments of Gastroenterology, Dermatology, Chinese Medicine, Urology, and Otolaryngology. To be eligible, subjects must have resided in Foshan for at least the past 5 years. Selection criteria for ischemic stroke cases were: sudden onset of focal neurological event with symptoms lasting for >24 hours and subsequent confirmation of infarct in the brain by CT or MRI and no history of stroke. Therefore, only patients with first-ever ischemic stroke (thrombotic or embolic) were considered. Fatal cases due to stroke were excluded because of ethical constraints. An eligible control did not have either history or clinical evidence indicating previous stroke and whose treatment at the outpatient department was not related to any cardiovascular disease, a malignant tumor, or diabetes. Subjects with a diagnosis of Alzheimer disease or who had been on long-term modification of diet for medical reasons were also excluded. Control subjects were matched to cases within 5 years of age and recruited during the same period as cases.

Sample Size and Participants

The required sample size was determined by assuming that 30% of Chinese adults drank ≥2 cups of tea daily with the relative risk of ischemic stroke being 0.5 at such level of intake.8 For a one-to-one case–control ratio at the 5% level of significance, the sample size needed to attain 90% power was 338 per group. To further account for refusal and withdrawal, 500 eligible cases and 600 age-matched control subjects were approached and invited to participate in the study. A total of 374 patients with stroke and 464 control subjects signed the consent form and completed the entire interview, representing an eventual response rate of 74.8% and 77.3%, respectively. There were no significant differences in age and gender distributions between those who consented and those who declined to participate.

Interview

The neurology wards of the 3 hospitals notified the first author within 2 days on admission of a patient with incident ischemic stroke. An appointment for interview was then arranged within 10 days or before discharge from the hospital. Control subjects were recruited and interviewed by the first author whenever available. All subjects were assured confidentiality and their right to withdraw without prejudice before obtaining their formal consent. The interviews, averaging 45 minutes in duration, took place in the neurology wards for cases and outpatient clinics for control subjects. When a patient was unable to provide answers as a result of the morbidity or MRI and no history of stroke. Therefore, only patients with first-ever ischemic stroke (thrombotic or embolic) were considered. Fatal cases due to stroke were excluded because of ethical constraints. An eligible control did not have either history or clinical evidence indicating previous stroke and whose treatment at the outpatient department was not related to any cardiovascular disease, a malignant tumor, or diabetes. Subjects with a diagnosis of Alzheimer disease or who had been on long-term modification of diet for medical reasons were also excluded. Control subjects were matched to cases within 5 years of age and recruited during the same period as cases.

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Questionnaire and Exposure Measurements

A structured questionnaire was administered face to face, usually in the presence of the participant’s next of kin to minimize recall error. Demographic and lifestyle characteristics solicited included age, gender, weight (in kilograms), height (in meters), education level (primary school, secondary school or above), smoking status (never-smoker, current/former smoker) and pack-years, and alcohol drinking status (non-drinker, drinker). Self-reported height and weight measurements and health conditions such as the presence of hypertension, hyperlipidemia, and diabetes were confirmed with medical records whenever available.

Information on habitual food consumption was obtained using a 125-item semiquantitative food frequency questionnaire developed for the southern Chinese population.19,20 This validated instrument covered most of the food items commonly consumed in south China. Frequency (per day/week/month) and the amount of intake were recorded in detail. The reference recall period for dietary variables was set at 1 year before interview. In addition, specific questions on tea drinking were taken from our previous prostate cancer study with established reliability and reproducibility.21 Subjects were first classified as “ever” or “never” tea drinkers (less than once per month). The ever-drinkers were asked to report their frequency of habitual intake (1 to 4 cups per month; 2 to 4 cups per week; 1 cup per day; 2 to 3 cups per day; 4 to 5 cups per day; 6 to 7 cups per day, >7 cups per day), duration of regular tea drinking (in years), types of tea drank (green, black, and oolong), and average quantity of dried tea leaves used for brewing tea in “jin” (500 g) and “liang” (50 g) per year. Frequency of liquid tea consumed was measured in terms of a standard cup (180 mL). The common method of preparation was to brew dry tea leaves using hot water without milk and sugar. For those who drank more than one type of tea, their reported ratio of consumption was used to estimate the respective frequency and amount of dried tea leaves for each type.

A further question on “lifelong physical activity involvement” was appended to the questionnaire defined as “doing active sports or vigorous exercise long enough to get sweaty, at least twice a week” over the entire life course. Response options were: never been much involved; previously active but not any more; active just recently; intermittently active; and always been involved.22

Statistical Analysis

Descriptive statistics were first applied to summarize participant characteristics and their tea consumption patterns. To investigate the effects of tea on the ischemic stroke risk, separate logistic regression analyses were performed for frequency of intake, duration of drinking, and quantity of tea leaves brewed. Tea drinking frequency was reclassified into 4 levels (<1 cup per week; 1 to 6 cups per week; 1 to 2 cups per day; >2 cups per day) with the lowest level of intake serving as the reference category. For total and type-specific tea leaves used, the 33th percentile and 66th percentile of these continuous variables among drinkers in the control group were used as cut points, resulting in 3 increasing levels of exposure, and less than one liang (50 g) per year was taken as the reference category. To further assess the dose–response relationship between long-term tea exposure and stroke risk, tests for linear trend were conducted for years of drinking and total and type-specific tea leaves brewed, treating them as continuous variables. Both crude and adjusted ORs and associated 95% CIs were reported.

Besides tea consumption, independent variables included in the logistic regression models were age, gender, education level, body mass index (<24 or ≥24 kg/m²), lifelong physical activity involvement, smoking status, smoking pack-years, alcohol drinking status, presence of hypertension, hyperlipidemia, and diabetes together with weekly dietary intake of meat, fish, poultry, fruit, and vegetables. These variables were either plausible risk factors from the literature or considered potential confounders according to the univariate analysis. Statistical analyses were undertaken using the STATA package release 10 (StataCorp).

Results

Table 1 profiles the characteristics of the participants. Both age and body mass index were similar between case and control groups across genders. A higher prevalence of hypertension and diabetes was found among the patients with stroke, who tended to smoke and had higher cumulative smoking exposure and who were less active over their life course. According to univariate t tests, the consumptions of total, green, and oolong tea leaves for brewing tea by control subjects were higher than those by patients with stroke in both genders (P<0.05) with the exception of black tea leaves (P=0.104 for male, P=0.752 for female). Control subjects appeared to have a longer exposure to tea as evident in their significantly higher mean duration of tea drinking (P<0.05) than the case group. Intakes of fruit and vegetable by control
subjects were also higher than cases (P<0.05). The data also revealed that men generally consumed more tea leaves and had a longer history of tea drinking than women (P<0.001). Characteristics of subjects by total tea drinking frequency and case–control status are provided in Supplemental Table I, available online at http://stroke.ahajournals.org.

Results of univariate and multivariate logistic regression analyses for tea drinking frequency are shown in Table 2. The probability values were obtained by likelihood ratio test for testing the overall significance of each categorical tea drinking variable in the multivariate models. Overall, a decrease in ischemic stroke risk was observed for those who drank at least one cup of tea per week (P<0.015) when compared with infrequent or nondrinkers, the reduction in risk being most effective by drinking one to 2 cups daily. In terms of type-specific frequency, the consumptions of green tea and oolong tea were significant (P<0.001), but not black tea (P=0.73).

Table 3 presents the effects of cumulative tea exposure and quantity of dried tea leaves brewed. A significant inverse association with ischemic stroke risk was evident for drinking duration, especially adults who had been drinking tea for >30 years (adjusted OR, 0.40; 95% CI, 0.25 to 0.64). With regard to tea leaf use, the dose–response relationship was significant overall (P for trend <0.001). In particular, those whose average yearly consumption of green tea leaves exceeded 3.2 kg exhibited the greatest reduction in stroke risk (adjusted OR, 0.12; 95% CI, 0.05 to 0.29). However, black tea appeared less beneficial than green and oolong teas, and indeed a slight, albeit nonsignificant, increase in ischemic stroke risk was found among drinkers using in excess of 1.9 kg of black tea leaves per year.

Separate analyses were further conducted for 2 strata (>20 years of tea drinking and <20 years of tea drinking) classified based on the 50th percentile of tea drinking duration among control subjects. Results are presented in Supplemental Table II. Inverse associations between risk of ischemic stroke and total tea consumption and type-specific tea consumption were observed for both strata, although more significant risk reductions were evident for the subgroup with longer tea exposure.

Finally, although proxy information was used in 22% of the cases, no differences were found between next of kin and the patient on tea consumption frequency, years of drinking, and dried tea leaves brewed. Details of the observed differences between the proxy and index person with respect to the

Table 1. Characteristic of Participants by Gender and Case–Control Status

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Male (n=474)</th>
<th>Female (n=364)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case (n=226)</td>
<td>Control (n=248)</td>
</tr>
<tr>
<td>Age, years</td>
<td>69.6 (8.0)</td>
<td>68.7 (7.0)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.9 (2.7)</td>
<td>23.1 (3.0)</td>
</tr>
<tr>
<td>Primary school education, n (%)</td>
<td>104 (46%)</td>
<td>88 (35.5%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>119 (52.7%)</td>
<td>71 (28.6%)</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>51 (22.6%)</td>
<td>23 (9.3%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>48 (21.2%)</td>
<td>8 (3.2%)</td>
</tr>
<tr>
<td>Alcohol drinker, n (%)</td>
<td>157 (69.5%)</td>
<td>147 (59.3%)</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td>162 (71.7%)</td>
<td>139 (56.1%)</td>
</tr>
<tr>
<td>Smoking pack-years</td>
<td>18.5 (22.1)</td>
<td>17.1 (22.2)</td>
</tr>
<tr>
<td>Lifelong physical activity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never been involved</td>
<td>71 (31.4%)</td>
<td>56 (22.6%)</td>
</tr>
<tr>
<td>Previously but not anymore</td>
<td>84 (37.2%)</td>
<td>53 (21.4%)</td>
</tr>
<tr>
<td>Active just recently</td>
<td>12 (5.3%)</td>
<td>15 (6.1%)</td>
</tr>
<tr>
<td>Intermittently active</td>
<td>22 (9.7%)</td>
<td>29 (11.7%)</td>
</tr>
<tr>
<td>Always been involved</td>
<td>37 (16.4%)</td>
<td>95 (38.3%)</td>
</tr>
<tr>
<td>Fruit intake, g/week</td>
<td>465 (636)</td>
<td>913 (765)</td>
</tr>
<tr>
<td>Vegetable intake, g/week</td>
<td>2109 (904)</td>
<td>2845 (1122)</td>
</tr>
<tr>
<td>Meat intake, g/week</td>
<td>660 (470)</td>
<td>645 (422)</td>
</tr>
<tr>
<td>Poultry intake, g/week</td>
<td>274 (294)</td>
<td>279 (293)</td>
</tr>
<tr>
<td>Fish intake, g/week</td>
<td>706 (525)</td>
<td>735 (617)</td>
</tr>
<tr>
<td>Duration of tea drinking, years</td>
<td>16.2 (15.8)</td>
<td>19.6 (16.6)</td>
</tr>
<tr>
<td>Dried tea leaves brewed, jin/year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All types</td>
<td>4.2 (4.5)</td>
<td>6.2 (6.1)</td>
</tr>
<tr>
<td>Green tea</td>
<td>0.8 (2.2)</td>
<td>2.4 (4.1)</td>
</tr>
<tr>
<td>Black tea</td>
<td>2.4 (4.0)</td>
<td>1.8 (3.9)</td>
</tr>
<tr>
<td>Oolong tea</td>
<td>0.8 (2.5)</td>
<td>1.7 (3.5)</td>
</tr>
</tbody>
</table>

*Mean (SD) unless indicated as n (%).
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Previous animal and in vitro studies and clinical trials have supported various types of tea, which enabled us to investigate their effect on ischemic stroke risk separately. Moreover, the underlying population consumes various types of tea, which enabled us to investigate their effect on ischemic stroke risk separately.

Our results indicated that the risk of ischemic stroke was significantly lower among subjects who regularly drank one to 2 cups of tea daily, especially green tea and oolong tea. Moreover, significant inverse dose–response relationships were found for years of drinking and average yearly quantity of tea leaves brewed. This protective effect of tea is supported by a growing body of literature from experimental studies. Previous animal and in vitro studies and clinical trials have suggested that tea drinking may protect against ischemic stroke by inhibiting the progress of atherosclerosis in the cerebral arteries and internal carotid arteries. As summarized in a recent review article, tea can prevent the formation of atherosclerosis by protecting the artery wall against high level of low-density lipoprotein plasma concentration, inhibiting the migration of monocytes to the atherosclerotic lesion, inhibiting proliferation of smooth muscle cells, and improving endothelial function.

This study suggests that continuous consumption of tea may reduce the risk of ischemic stroke, and the risk can be further reduced by longer-term and higher-dose tea exposure, especially for green tea and oolong tea. These findings are consistent with the results from 2 previous Japanese studies of green tea. Contrary to 2 prospective cohort studies conducted in Finland and The Netherlands, we did not find a clear association between black tea consumption and the risk of ischemic stroke. A plausible reason is that, unlike Western countries, our study population commonly drinks a concentrated postfermented tea called “Pu-erh,” which has a distinctive dark color and flavor. Consequently, the apparent lack of significant effect observed for black tea represented a combination of “Pu-erh” tea mixed with other subtypes of black tea. Similarly, a prospective cohort study conducted in the United States found no significant association between black tea consumption and the risk of stroke.

Results of this case–control study could potentially be affected by several sources of bias. First, the potential beneficial effect of tea drinking has not been established in China so that information bias was unlikely. Also, the habitual tea consumption pattern should not be affected by

### Table 2. Risk of Ischemic Stroke for Frequency of Tea Drinking

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Case, n (%)</th>
<th>Control, n (%)</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>Adjusted OR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 cup/week</td>
<td>199 (53.2%)</td>
<td>192 (41.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–6 cups/week</td>
<td>22 (5.9%)</td>
<td>34 (7.3%)</td>
<td>0.62</td>
<td>(0.35, 1.11)</td>
<td>0.55</td>
<td>(0.28, 1.10)</td>
</tr>
<tr>
<td>1–2 cups/day</td>
<td>45 (12.0%)</td>
<td>111 (23.9%)</td>
<td>0.39</td>
<td>(0.26, 0.58)</td>
<td>0.30</td>
<td>(0.19, 0.49)</td>
</tr>
<tr>
<td>&gt;2 cups/day</td>
<td>108 (28.9%)</td>
<td>127 (27.4%)</td>
<td>0.82</td>
<td>(0.59, 1.13)</td>
<td>0.61</td>
<td>(0.40, 0.94)</td>
</tr>
</tbody>
</table>

*Separate models for total and each type of tea adjusted for age, gender, body mass index, education level, lifelong physical activity involvement, smoking status, smoking pack-years, alcohol drinking status, presence of hypertension, hyperlipidemia and diabetes, and weekly dietary intake of meat, fish, poultry, fruit, and vegetables.
the case–control status. Dietary assessment was based on self-report using a validated and reliable questionnaire for the southern Chinese population. However, responses from the patients with stroke would inevitably incur some recall bias due to possible memory and/or cognitive loss from stroke. Therefore, face-to-face interviews were conducted in the presence of their next of kin to increase the response rate and to improve the accuracy of their answers. In addition, all interviews were conducted by the same investigator (first author) to eliminate interinterviewer bias. Selection bias was unavoidable because all participants were voluntary and the hospital-based control subjects were not randomly selected from the community. The 3 participating hospitals serve the entire Foshan catchment region so that our subjects were representative of the target population. Residual confounding is another possibility that cannot be ignored. Plausible risk factors have been accounted for and adjusted in the multivariate logistic regression analyses. Moreover, the correlation matrix for total and 3 types of tea, fruit intake, vegetable intake, and smoking exposure in Supplemental Table IV indicates little association between tea consumption variables and these potential confounders. There is also no evidence from the literature supporting habitual tea consumption as a marker of a healthy lifestyle among southern Chinese. Nevertheless, further replications of the study are recommended before generalizing the findings to other populations and countries.

### Summary

An inverse association was found between tea consumption and the risk of ischemic stroke in a southern Chinese population with a significant dose–response relationship for drinking green tea and oolong tea. Tea is a safe and inexpensive beverage. Its consumption should be encouraged in the meantime because of the potential benefit in stroke prevention.

### Disclosures

None.

### References

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doi: 10.1161/STROKEAHA.109.548586

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