Alcohol and Acute Ischemic Stroke Onset
The Stroke Onset Study

Elizabeth Mostofsky, MPH; Mary R. Burger, MD; Gottfried Schlauf, MD, PhD; Kenneth J. Mukamal, MD, MPH; Wayne D. Rosamond, PhD; Murray A. Mittleman, MD, DrPH

Background and Purpose—Previous research suggests that regular heavy alcohol consumption increases the risk for ischemic stroke, whereas frequent light to moderate alcohol intake may decrease the risk. However, the risk of ischemic stroke associated with transient exposure to alcohol remains unclear. In this study, we used a case–crossover approach to test the hypothesis that alcohol consumption affects the acute risk of ischemic stroke, to determine the length of time between alcohol intake and the onset of symptoms (induction time), and to examine whether the risk varies by the type of alcohol.

Methods—In this multicenter study, we interviewed 390 patients (209 men, 181 women) between January 2001 and November 2006 (median 3 days after stroke). Alcohol consumption in the hour before stroke symptoms was compared with its expected frequency based on the usual frequency of alcohol consumption over the prior year.

Results—Of the 390 patients, 248 (64%) reported alcohol consumption in the prior year, 104 within 24 hours and 14 within 1 hour of stroke onset. The relative risk of stroke in the hour after consuming alcohol was 2.3 (95% CI, 1.4 to 4.0; P=0.002). The relative risks were similar for different types of alcoholic beverages and when the sample was restricted to those who were not simultaneously exposed to other potential triggers.

Conclusions—The risk of stroke onset is transiently elevated in the hour after alcohol ingestion. (Stroke. 2010;41:1845-1849.)

Key Words: alcohol • case–crossover • cerebrovascular disorders • epidemiology • stroke

Moderate^{1} and high^{2,4} intakes of alcohol have been documented to have acute potentially deleterious physiological effects within hours after consumption, including impaired fibrinolysis^{2,3} and increased platelet activation,^{4} blood pressure, and heart rate.^{1} On the other hand, moderate consumption of alcohol has been associated with protective effects within hours,^{5–7} weeks,^{8,12} or years,^{13–15} including enhanced fibrinolytic activity^{7,8} and improvements in lipid profile,^{12} inflammatory markers,^{8,11} flow-mediated vasodilatation,^{5,6} soluble vascular adhesion molecules,^{11,14} insulin sensitivity,^{9,15} and adipokines.^{9,14} However, only a few studies^{16–18} have examined the risk of ischemic stroke associated with transient exposure to alcohol.

In this study, we used a case–crossover approach to test the hypothesis that alcohol consumption affects the acute risk of ischemic stroke, to determine the length of time between alcohol intake and the onset of symptoms (induction time), and to examine whether the risk varies by the type of alcohol.

Methods

Study Population
The Stroke Onset Study was conducted in 3 medical centers (Beth Israel Deaconess Medical Center, Boston, Mass; University of North Carolina Hospitals, Chapel Hill, NC; Vancouver Island Health Authority, Victoria, British Columbia, Canada). Between January 2001 and November 2006, 390 patients (209 men and 181 women) were interviewed a median of 3 days (range, 0 to 14 days) after sustaining an acute ischemic stroke. Research staff identified eligible patients by reviewing admission logs and charts of patients admitted to each hospital’s stroke service. Additionally, patients with new onset of an acute neurological syndrome compatible with stroke were screened on admission to emergency departments. Presumed stroke etiology was classified using an abbreviated Trial of Org 10172 in Acute Stroke Treatment system.^{19}

Study personnel using standardized abstraction forms recorded data on demographics, medical history, and admission laboratory results. Eligible participants had a neurologist-confirmed diagnosis of acute ischemic stroke either by clinical diagnosis or appropriate imaging studies, were English-speaking, and free of dementia before the index event. Patients were excluded if they could not identify the time of onset of their stroke symptoms or if the treating clinician deemed them unable to complete the structured interview because they were cognitively impaired, had poor memory around the time of the stroke, experienced aphasia, or they were too ill to complete the structured interview that lasted 30 to 45 minutes. Across all sites, 43% of patients with confirmed ischemic stroke met all inclusion criteria. Of these, 83% agreed to participate, 5.5% refused, and 12.5% were discharged from the hospital before the interviewers were able to approach them. The protocol was approved by the Clinical Science
Reliability and Validity of the Questionnaire

The test–retest reliability of the Stroke Onset Study questionnaire was assessed in 25 patients who were reinterviewed up to 6 days after their initial interview. The intraclass correlation for the usual frequency of alcohol consumption was excellent (0.84), and there was perfect agreement for reporting of any alcohol consumption during the past year and during each of the first 2 hours before stroke onset (κ = 1.0). In the subset of 181 subjects interviewed at Beth Israel Deaconess Medical Center who had high-density lipoprotein cholesterol levels measured at the time of hospitalization, the partial correlation between estimated alcohol consumption and high-density lipoprotein cholesterol level adjusting for sex, age, race, smoking, education, and physical activity was 0.35 (P = 0.003), comparable to that found in the Second National Health and Nutrition Examination Survey.20

Study Design

The Stroke Onset Study used a case–crossover study design to assess the change in risk of acute ischemic stroke onset during a brief “hazard period” after consumption of alcohol. In the case–crossover design, control information for each patient is based on his or her own past exposure experience. Self-matching eliminates confounding by risk factors that are constant within individuals over the sampling period but differ between subjects. Alcohol use in the hazard period, the 1-hour period immediately before the onset of ischemic stroke symptoms, was compared with its expected frequency based on control data obtained from the patients. We used the usual frequency of alcohol consumption over the year before stroke to estimate its expected frequency in an average 1-hour period.

Statistical Analysis

Each patient in a case–crossover study forms his or her own stratum and thus is his or her own control.21,22 The ratio of the observed exposure frequency in the hazard period to the expected frequency was used to calculate estimates of the rate ratio as a measure of relative risk (RR). We multiplied the usual annual frequency of alcohol consumption by the hypothesized window of its physiological effect (1 hour in the primary analysis) to estimate the amount of person-time exposed to alcohol. The unexposed person-time was calculated by subtracting this value from the number of hours in 1 year. The data were analyzed using methods for cohort studies with sparse data in each stratum.

To estimate the length of time from alcohol consumption to the onset of ischemic stroke, RR were calculated by comparing exposure within different hypothesized windows of its physiological effect with the estimated person-time exposed to alcohol in the previous year. We conducted stratified analyses to assess the effect of drink type (beer, wine, liquor), sex, age (<65 years of age versus ≥65 years of age), smoking status (current smokers versus nonsmokers), and stroke etiology and compared the RRs by means of a test for homogeneity.23

Results

The characteristics of the Stroke Onset Study patients are presented in the Table. Of the 390 patients with acute ischemic stroke, 248 (64%) reported that they had consumed alcohol in the prior year (wine, n = 45; beer, n = 29; liquor, n = 32; >1 type, n = 142). Compared with nondrinkers, subjects who reported alcohol consumption were more likely to be male and to have ever smoked cigarettes. Among the 248 subjects who drank alcohol in the prior year, 47 (12%) reported drinking at least 1 serving of alcohol per day, 38 (10%) reported drinking at least once per week, and 163 (66%) reported drinking at least once per month. The median frequency of consumption among drinkers in the prior year

<table>
<thead>
<tr>
<th>Study Population*</th>
<th>Alcohol Drinkers (n=248)</th>
<th>Nondrinkers (n=142)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>68±14.5</td>
<td>69±13.7</td>
<td>0.11</td>
</tr>
<tr>
<td>Male</td>
<td>143 (58%)</td>
<td>66 (47%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>Never</td>
<td>72 (29%)</td>
<td>56 (39%)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>122 (49%)</td>
<td>63 (44%)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>54 (22%)</td>
<td>23 (16%)</td>
<td></td>
</tr>
<tr>
<td>Obesity (body mass index ≥30 kg/m²)†</td>
<td>59 (24%)</td>
<td>31 (22%)</td>
<td>0.68</td>
</tr>
<tr>
<td>Diabetes</td>
<td>56 (23%)</td>
<td>39 (27%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>101 (41%)</td>
<td>45 (32%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>152 (61%)</td>
<td>100 (70%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>32 (13%)</td>
<td>22 (15%)</td>
<td>0.48</td>
</tr>
<tr>
<td>History of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>36 (15%)</td>
<td>14 (10%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Stroke</td>
<td>41 (17%)</td>
<td>32 (23%)</td>
<td>0.14</td>
</tr>
<tr>
<td>TIA</td>
<td>29 (12%)</td>
<td>18 (13%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>11 (8%)</td>
<td>31 (13%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Carotid endarterectomy</td>
<td>2 (1%)</td>
<td>5 (2%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Stroke etiology‡</td>
<td></td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>Small vessel</td>
<td>67 (29%)</td>
<td>44 (37%)</td>
<td></td>
</tr>
<tr>
<td>Large vessel</td>
<td>46 (20%)</td>
<td>21 (18%)</td>
<td></td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>57 (25%)</td>
<td>24 (20%)</td>
<td></td>
</tr>
<tr>
<td>Other/undetermined</td>
<td>60 (26%)</td>
<td>32 (26%)</td>
<td></td>
</tr>
</tbody>
</table>

*Mean±SD or no. (%).
†There was no data available on body mass index for 7 subjects.
‡At 1 of the centers, stroke etiology was not determined (n = 39).
MI indicates myocardial infarction; TIA, transient ischemic attack.
was 2.0 times per week. Subjects reported that they typically drank small amounts each time (median = 1 drink) and only 13 reported typically drinking >2 servings.

There were 169 subjects who reported exposure during the week before stroke, 104 subjects drank alcohol within 24 hours of stroke onset, and 14 drank within 1 hour of stroke onset. We found that within 1 hour after alcohol consumption, the risk of stroke onset was 2.3-fold higher (95% CI, 1.4 to 4.0; *P* = 0.002) compared with periods of nonuse. The RR was 1.6 (95% CI, 1.0 to 2.5; *P* = 0.05) in the second hour after drinking and returned to baseline thereafter (Figure 1). By 24 hours, there was a 30% lower risk (RR = 0.7, 95% CI, 0.5 to 0.9; *P* = 0.02).

Among the 14 participants who consumed alcohol in the hour before stroke onset, 7 drank liquor, 5 drank beer, and 2 drank wine. The RR for alcohol consumption in the hour before stroke onset was strongest for liquor and weakest for wine, although the difference was not statistically significant (*P* for interaction = 0.28; Figure 2). The RRs for alcohol consumption in the hour before stroke did not vary by sex, age, smoking status, or stroke etiology (*P* for interaction = 0.62, 0.62, 0.12, and 0.43, respectively).

Among the 248 participants exposed to alcohol in the prior year, 63 participants were exposed to other potential triggers in the hour before stroke onset. Of the 14 people exposed to alcohol in the hour before stroke onset, 4 were also exposed to vigorous physical activity and 1 drank a caffeinated beverage. When we conducted an analysis excluding the 63 people exposed to any potential stroke trigger in the hour before stroke onset did not meaningfully alter the results.

The mean usual frequency of alcohol consumption during the past year was 4.42 times per week, similar to the mean frequency of reported alcohol consumption during the past week (4.23). In a sensitivity analysis using each patient’s reported frequency of consumption in the past week as the control information, the risk of ischemic stroke onset was 3.3-fold higher (95% CI, 1.6 to 8.7), respectively. Consistent with our data, Gorelick et al. found that moderate (151 to 300 g) and heavy (>300 g) consumption of alcohol within the week before stroke onset is associated with a significantly higher risk of stroke with adjusted ORs of 3.6 (95% CI, 1.7 to 7.8) and 3.7 (95% CI, 1.6 to 8.7), respectively. Consistent with our data, Hillbom et al. found that moderate (151 to 300 g) and heavy (>300 g) consumption of alcohol within the week before stroke onset is associated with a significantly higher risk of stroke with adjusted ORs of 3.6 (95% CI, 1.7 to 7.8) and 3.7 (95% CI, 1.6 to 8.7), respectively. Consistent with our data, Hillbom et al. found that moderate (151 to 300 g) and heavy (>300 g) consumption of alcohol within the week before stroke onset is associated with a significantly higher risk of stroke with adjusted ORs of 3.6 (95% CI, 1.7 to 7.8) and 3.7 (95% CI, 1.6 to 8.7), respectively. Consistent with our data, Hillbom et al. found that moderate (151 to 300 g) and heavy (>300 g) consumption of alcohol within the week before stroke onset is associated with a significantly higher risk of stroke with adjusted ORs of 3.6 (95% CI, 1.7 to 7.8) and 3.7 (95% CI, 1.6 to 8.7), respectively.
Although some studies reported no association with ischemic or hemorrhagic stroke, recent comprehensive reviews and indicate a decreased risk of ischemic stroke and a higher risk of hemorrhagic stroke associated with light to moderate consumption.

Integrating the short-term effects observed here with other studies on alcohol use and long-term risk is difficult. Although speculative, it is possible that the transiently increased stroke risk from moderate alcohol consumption may be outweighed by the health benefits for the next 24 hours, but consuming multiple drinks at once may result in a sharp increase in acute risk with potential increased long-term risk as well. Mukamal and colleagues found that, compared with complete abstinence from alcohol, light consumption (<1 drink daily) is not associated with stroke risk, moderate alcohol consumption (1 to 2 drinks daily) is protective, and intake of >2 drinks per day is associated with an increased risk of ischemic stroke. Our finding of an acute detrimental effect and a suggestion of a decreased risk over the 24-hour period after alcohol consumption seem consistent with these findings. For example, one may hypothesize that over time, individuals who drink large amounts infrequently primarily experience the acute detrimental effect, whereas subjects who drink small amounts frequently may still experience a transient increase in risk, but this may be offset in part by the subsequent reduction in risk that follows.

There are some limitations to our study. Because the case–crossover design uses subjects as their own controls, there can be no confounding by risk factors that are stable over time. Confounding by factors that change over time within individuals can occur. However, excluding subjects reporting other potential triggers in the hour before stroke onset did not materially alter the results. In an effort to minimize reporting bias, efforts were made to ensure the patient’s privacy during the interview. We used a standardized structured interview and patients were not informed of the duration of the hypothesized hazard period. Because most of the participants drank small amounts of alcohol in the hour before stroke onset, we could not examine the acute effects of different doses of alcohol. We had limited power to evaluate the effect of beverage type because few participants were consuming multiple drinks at once. The risk rapidly returned to baseline and intake of >2 drinks per day is associated with an increased risk of hemorrhagic stroke associated with light to moderate alcohol consumption (1 to 2 drinks daily) is protective, and intake of >2 drinks per day is associated with an increased risk of ischemic stroke. Our finding of an acute detrimental effect and a suggestion of a decreased risk over the 24-hour period after alcohol consumption seem consistent with these findings. For example, one may hypothesize that over time, individuals who drink large amounts infrequently primarily experience the acute detrimental effect, whereas subjects who drink small amounts frequently may still experience a transient increase in risk, but this may be offset in part by the subsequent reduction in risk that follows.

Summary
In conclusion, we found that the risk of ischemic stroke was transiently elevated for 2 hours after drinking as little as 1 serving of alcohol. The risk rapidly returned to baseline and was modestly lower by 24 hours. When examined in the context of long-term studies of alcohol consumption, the net clinical impact on ischemic stroke risk appears to depend on the frequency and quantity of alcohol consumption. Definitive evidence would require a long-term clinical trial, although such a trial would be logistically difficult and is unlikely to be carried out in the near future.

Acknowledgments
We thank Cindy Aiello for outstanding administrative assistance.

Sources of Funding
This work was supported by an Established Investigator Grant (0140219N) from the American Heart Association, Dallas, Texas, and T32-A1007535-11.

Disclosures
None.

References


Alcohol and Acute Ischemic Stroke Onset: The Stroke Onset Study
Elizabeth Mostofsky, Mary R. Burger, Gottfried Schlaug, Kenneth J. Mukamal, Wayne D. Rosamond and Murray A. Mittleman

*Stroke*. 2010;41:1845-1849; originally published online July 15, 2010;
doi: 10.1161/STROKEAHA.110.580092

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 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/41/9/1845

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2016/03/31/STROKEAHA.110.580092.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/
背景和目的：早前的研究提示规律性大量饮酒会增加缺血性卒中的风险，而经常性的少量饮酒则能减少其风险。然而，一次性饮酒的缺血性卒中风险仍不明确。本研究采用病例交叉研究来检验饮酒对急性缺血性卒中风险的影响，以了解饮酒开始至症状出现的时程（诱发时间）及观察不同种类酒精饮料对卒中风险的影响。方法：本研究设于2001年1月至2006年11月间，共询问390名患者（男性209人，女性181人，中位时间为卒中发病后3天）。基线时在卒中症状出现前1小时内的饮酒频率与预期频率进行比较。结果：390名患者中，248例（64%）在前一年内饮酒，104例在卒中发病前24小时内曾有饮酒，14人在发病前1小时内曾有饮酒。饮酒后1小时内卒中发生的相对危险为2.3（95%可信区间为1.4-4.0；P=0.002）。当严格控制样本于那些并未同时暴露于其他诱因的患者时，不同种类酒精饮料具有相类似的相对危险度。结论：饮酒后1小时内卒中发生的风险会短暂地升高。关键词：酒精，病例交叉研究，脑血管病，流行病学，卒中


方法

研究人群

卒中起病研究 (Stroke Onset Study, SOS) 在三个医学中心（马萨诸塞州波士顿的Beth Israel Deaconess医学中心，北卡罗来纳州的北卡罗来纳大学医院，加拿大不列颠哥伦比亚省温哥华岛卫生局）中进行。在2001年1月至2006年11月期间，共纳入390例患者（男性209例，女性181例），在急性缺血性卒中发病后（中位数3天，范围在0-14天）进行访谈。研究人员通过回顾各医院卒中中心收治患者的入院目和病历记录明确入组患者。另外，对急诊入院时符合新发急性卒中表现的患者进行筛查。患者卒中的病因学诊断使用TOAST分型[19]。

研究人员使用标准化简要表格记录患者的人口统计学资料、既往史和入院时实验室结果等数据。合格的参与者应符合神经科临床诊断或相关的影像学检查明确的急性缺血性卒中诊断，语言为英语，在卒中事件前无痴呆。排除标准包括：无法明确卒中症状的发生时间；或因认知损害、不能回忆卒中发病时间、有失语或疾病危重无法完成持续30-45
Mostofsky et al  Alcohol and Stroke Onset: The Stroke Onset Study

分钟访谈等原因而无法完成结构性访谈。所有中心中，43% 为明确的缺血性卒中患者符合入选标准，其中 83% 患者同意入组，5.5% 被拒绝入组，12.5% 患者在接触前已出院。研究方案经各分中心伦理委员会批准并获得每位患者的知情同意。

访谈人员使用结构性问卷询问患者出现症状的时间及起病前一年内是否饮酒。要求所有曾经有饮酒的患者提供末次酒精饮料摄入时间、前一年里饮酒的频率、每次饮酒量和饮酒种类（啤酒、葡萄酒或烈性酒）等信息。一份酒精量的定义为 12 盎司啤酒或 4 盎司葡萄酒或 1.5 盎司烈性酒的直接或混合饮用。患者同时被要求提供最后一次其他潜在诱因（包括咖啡因、烟草、大麻、可卡因、应激、愤怒和体力活动）的暴露时机及最近一年中这些诱因的暴露频率。其他在访谈中收集的信息还包括药物的使用和卒中当天的症状。

问卷的信度和效度

在 25 名患者中进行 SOS 问卷的重测信度评估，他们在首次访谈后 6 天再次接受访谈。饮酒的既往频率在组内的相关性高度一致（0.84），对最近一年内饮酒的报告也具有良好的一致性（k=1.0）。181 例在 Beth Israel Deaconess 医学中心住院的患者接受了高密度脂蛋白胆固醇的检测，校正性别、年龄、种族、吸烟史、教育、体力活动等因素后，饮酒的估计量与高密度脂蛋白水平存在相关性（0.35，P=0.003），与第二次国家健康与营养检验调查一致[20]。

研究设计

SOS 使用了病例交叉对照设计，来评估饮酒后短时间“危险期”中，急性卒中发生风险的变化。在病例交叉设计中，每位患者自身既往所存在的暴露作为其对照信息。自身对照控制了患者在研究期间持续存在的因素，将患者危险期，即缺血性卒中症状发病前 1 小时的饮酒情况与基于控制数据中的预期频率相比较。我们使用卒中前一年中饮酒的频率来估计其平均 1 小时的频率。

统计分析

病例交叉研究中的每位患者形成了其各自独立的分层，并进行自身对照[21,22]。所观察到的危险期内的暴露频率与计算所得的预期频率的比率作为相对危险度（RR）。我们将既往每年饮酒频率乘以理论性生理作用的时间窗（初步分析为 1 小时）来估计暴露于酒精频率的人 / 时数，并将未暴露的人 / 时数在一年中减去。每层中所缺失数据的分析采用队列研究方法。

为了明确饮酒至缺血性卒中发生的时间长度，RR 值的计算比较了按生理作用使用不同假设时间窗的饮酒暴露和估计过去的暴露量 / 时数。我们将患者卒中前一周内的饮酒量作为控制信息。我们无法明确酗酒与缺血性卒中的关系，因为仅有 1 例患者在卒中发生前 1 小时内饮酒 2 个单位。以上检验均为双侧检验。

结果

SOS 中患者的特征见表。据报道，在 390 例急性缺血性卒中患者中，有 248 例 (64%) 在近一年中饮酒者（n=248）非饮酒者（n=142）P 值

| 年龄，岁 | 68 ± 14.5 | 69 ± 13.7 | 0.11 |
| 性别，男 | 143 (58%) | 66 (47%) | 0.03 |
| 吸烟史 | 0.09 |
| 从未 | 72 (29%) | 56 (39%) | 0.68 |
| 既往 | 122 (49%) | 63 (44%) | 0.28 |
| 目前 | 54 (22%) | 23 (16%) | 0.08 |
| 肥胖（BMI ≥ 30 kg/m²）† | 59 (24%) | 31 (22%) | 0.07 |
| 糖尿病 | 56 (23%) | 39 (27%) | 0.28 |
| 高脂血症 | 101 (41%) | 45 (32%) | 0.07 |
| 高血压 | 152 (61%) | 100 (70%) | 0.07 |
| 心房颤动 | 32 (13%) | 22 (15%) | 0.48 |

* 数据以均数 ± 标准差或数量（%）形式表示。
† 7 例患者缺乏体重指数 (BMI) 数据。
‡ 在 1 个中心未进行卒中病因学诊断 (n=39)。
饮酒（其中葡萄酒45例、啤酒29例、烈性酒32例、大于一种142例）。与未饮酒者相比，饮酒者更倾向于为男性和吸烟者。在248例发病前一年里饮酒的患者中，47例(12%)饮酒至少每日≥1个单位，38例(10%)至少每周一次，163(66%)至少每月一次。患者最近一年中饮酒频率的中位数为每周2.0次，自述每次饮酒量较少(中位数为1个单位)，仅13例饮酒量超过2个单位。

169例患者在卒中前一周内有饮酒，104例则在卒中发生前24小时内饮酒，其中1小时内有14例。饮酒后1小时内卒中发生的危险是未饮酒者的2.3倍(95%可信区间[CI]: 1.440; P=0.002)。饮酒后第2小时的卒中发生的相关危险为1.6(95%CI, 1.0-2.5; P=0.05)，之后相对危险回落至基线水平(图1)。在24小时内，相对风险则下降了30%(RR=0.7, 95%CI, 0.5-0.9; P=0.02)。

在卒中发生前1小时内饮酒的14例中，7人饮烈性酒，5人饮啤酒，2人饮葡萄酒。卒中前1小时内饮酒的相对危险高于烈性酒，但没有达到统计学意义(交互后的P值为0.28; 图2)。卒中前1小时内饮酒的相对危险与性别、年龄、吸烟史或卒中病因无关(交互后的P值分别为0.62、0.62、0.12和0.43)。

在248例一年内饮酒的患者中，63例在卒中发生前1小时内暴露于其他潜在的诱因。在卒中发生前1小时内饮酒的14例中，4例曾进行剧烈的体力活动，1例摄入含有咖啡因的饮料。当排除了1小时内具有其他潜在卒中诱因的63例患者后，研究结果与之前相似。

患者在最近的一年中平均饮酒频率为每周4.42次，与最近一周内的平均饮酒频率相似(4.23次)。用每位患者所报告的最近一周的平均饮酒频率为对照所作的灵敏度分析，饮用至少1个单位酒后1小时内的缺血性卒中发病风险是未饮酒期的3.3倍(95%CI, 1.2-9.3; P=0.03)。排除1例患者在卒中发生前2小时内摄入2个单位的酒精，分析结果无明显变化。

讨论
本研究发现饮酒后1小时内缺血性卒中的风险将会短暂性地上升，其风险是未饮酒时的2.3倍。本研究所显示的饮酒后的急性损害作用，与早前研究的发现一致[17,18]。卒中风险在饮酒3小时后回落至基线水平，并于24小时到达低点。

个别研究进行了酒精作为缺血性[16-18,24]和出血性卒中[25]的诱因的研究。如Hillborn等[18]发现卒中前一周内中度(151-300g)至重度(>300g)饮酒是卒中发生的显著高危因素，校正后的OR值为3.6(95%CI, 1.7-7.8)，与本研究相一致。但Gorelick等[24]研究表明，校正了包括吸烟在内的协同暴露因素后，饮酒后24小时内的缺血性卒中风险未见明显升高。


与饮酒的急性作用相反，一系列证据显示长期大量饮酒与缺血性[27,28]和出血性[28-30]卒中的风险增加相关。然而，少-中等量饮酒研究的相关证据并
Mukamal et al.  

Alcohol and Stroke Onset: The Stroke Onset Study