Brief Report

Smoking and Risk of Ischemic Stroke in Young Men

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Background and Purpose—There is a strong dose–response relationship between smoking and risk of ischemic stroke in young women, but there are few data examining this association in young men. We examined the dose–response relationship between the quantity of cigarettes smoked and the odds of developing an ischemic stroke in men under age 50 years.

Methods—The Stroke Prevention in Young Men Study is a population-based case–control study of risk factors for ischemic stroke in men ages 15 to 49 years. The χ^2 test was used to test categorical comparisons. Logistic regression models were used to calculate the odds ratio for ischemic stroke occurrence comparing current and former smokers to never smokers. In the first model, we adjusted solely for age. In the second model, we adjusted for potential confounding factors, including age, race, education, hypertension, myocardial infarction, angina, diabetes mellitus, and body mass index.

Results—The study population consisted of 615 cases and 530 controls. The odds ratio for the current smoking group compared with never smokers was 1.88. Furthermore, when the current smoking group was stratified by number of cigarettes smoked, there was a dose–response relationship for the odds ratio, ranging from 1.46 for those smoking <11 cigarettes per day to 5.66 for those smoking 40+ cigarettes per day.

Conclusions—We found a strong dose–response relationship between the number of cigarettes smoked daily and ischemic stroke among young men. Although complete smoking cessation is the goal, even smoking fewer cigarettes may reduce the risk of ischemic stroke in young men. **(*Stroke*. 2018;49:00-00. DOI: 10.1161/STROKEAHA.117.018859.)**

Key Words: risk factors ■ smoke ■ smoking ■ stroke ■ tobacco products

Incidence of ischemic stroke (IS) in young adults is increasing.[1] In addition, cigarette smoking, a modifiable risk factor for IS, has been on the rise among young adults.[1–4] Our prior research among young women suggests a strong dose–response relationship between smoking and risk of IS,[5] but there are few studies examining this association in young men. Because of potential interactions between smoking and hormonal milieu, a separate examination of this issue in men is important. The extension of our study to men allows us to address this issue. In this study, we examine the dose–response relationship between the quantity of cigarettes smoked daily and the odds of developing an IS in men under age 50 years.

Methods

To minimize the possibility of unintentionally sharing information that can be used to reidentify private information, a subset of the data generated for this study is available at dbGaP and can be accessed at https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000292.v1.p1.

The Stroke Prevention in Young Men Study is a population-based case–control study of risk factors for IS in men ages 15 to 49 years. All cases were recruited within 3 years of stroke between 2003 and 2007. Controls were identified by random-digit dialing and were balanced with cases for geographic region of residence, age within 5 years, and ethnicity. Never smokers were defined as those who had not smoked >100 cigarettes or 5 packs in their lifetime. Current smokers were defined as those who had smoked >100 cigarettes in their lifetime and also had smoked in the 30 days preceding their stroke (for cases) or interview (for controls). Former smokers were defined as those who had smoked >100 cigarettes in their lifetime but had not smoked in the 30 days before their stroke/interview. Standardized interviews were conducted to collect data on smoking and other vascular risk factors. Further details on study methods have been published.[5]

The study was approved by the University of Maryland at Baltimore Institutional Review Board, and all participants gave informed consent.

Statistical Methodology

Statistical analysis was conducted using SAS version 9.4. The χ^2 test was used to test categorical comparisons. Logistic regression models were used to calculate the odds ratio for IS occurrence comparing smokers to never smokers. In the first model, we adjusted solely for age. In the second, fully-adjusted, model, we adjusted for potential confounding factors, including age, race, education, hypertension, myocardial infarction, angina,

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Table 1. Demographic Characteristics of Participants

Factor	Category	Cases n (%) (n=615)	Controls n (%) (n=530)	*P* Value*	Current Smokers† n (%) (n=160)	Former and Never Smokers† n (%) (n=370)	*P* Value*
Age, y	<18	2 (0.3)	1 (0.2)	0.01	0 (0)	1 (0.3)	0.22
	18–24	11 (1.8)	10 (1.9)		6 (3.8)	4 (1.1)	
	25–34	45 (7.3)	72 (13.6)		18 (11.2)	54 (14.5)	
	35–49	557 (90.6)	447 (84.3)		136 (85.0)	311 (84.1)	
Race	White	333 (54.2)	305 (57.6)	0.27	68 (42.5)	237 (64.1)	<0.001
	Black	258 (42.0)	199 (37.5)		86 (53.8)	113 (30.5)	
	Other	24 (3.8)	26 (4.9)		6 (3.7)	20 (5.4)	
Education	<12	96 (15.6)	45 (8.5)	<0.001	28 (17.5)	17 (4.6)	<0.001
	≥12	519 (84.4)	485 (91.5)		132 (82.5)	353 (95.4)	
Hypertension	Yes	288 (46.8)	121 (22.8)	<0.001	41 (25.6)	80 (21.6)	0.31
Diabetes mellitus	Yes	115 (18.7)	30 (5.7)	<0.001	10 (6.2)	20 (5.4)	0.70
Myocardial infarction	Yes	38 (6.2)	6 (1.1)	<0.001	4 (2.5)	2 (0.5)	0.05
Angina	Yes	56 (9.1)	27 (5.1)	0.01	14 (8.8)	13 (3.5)	0.12
Body mass index	<30	365 (59.4)	368 (69.4)	<0.001	120 (75.0)	248 (67.0)	0.07
	≥30	250 (40.6)	162 (30.6)		40 (25.0)	122 (33.0)	

*χ^2.
†Controls only.

diabetes mellitus, and body mass index. Interaction terms were used to examine potential effect modification by other risk factors. Statistical tests were 2-tailed, and $P<0.05$ was considered statistically significant.

Results

Among the participants, 615 of 625 cases and 530 of 537 controls had complete data for all covariates, leaving a final study population of 1145 subjects. Cases were less educated and were more likely to have hypertension, diabetes mellitus, myocardial infarction, angina, and obesity (body mass index >30; all $P<0.05$). Among controls, current smokers were less educated and were more likely to be black than their nonsmoking counterparts (all $P<0.05$; Table 1).

Table 2 shows that in the age-adjusted model, the odds ratio for the current smoking group compared with never smokers was 1.88 (95% confidence interval, 1.44–2.44). Furthermore, when the current smoking group was stratified by number of cigarettes smoked, there was a dose–response relationship for the odds ratio, ranging from 1.46 (95% confidence interval, 1.04–2.06) for those smoking <11 cigarettes per day to 5.66 (95% confidence interval, 2.14–14.95) for those smoking 40+ cigarettes per day. In the fully-adjusted model, there is a similar dose response observed but with slightly lower odds ratios. In the age-adjusted model, the odds ratio for the former smoking group compared with never smokers was 1.42 (95% confidence interval, 1.01–1.99), with similar results for the fully-adjusted model (Table 2).

Discussion

Our study demonstrates a strong dose–response between amount of cigarettes smoked and risk of IS in young men.

Table 2. Odds Ratio for Ischemic Stroke by Smoking Status

	Cases (n=615)	Controls (n=530)	Model 1* OR	95% CI	Model 2† OR	95% CI
Never smokers	239	286	…	…	…	…
Former smokers	108	84	1.42	1.01–1.99	1.33	0.93–1.90
Current smokers	268	160	1.88	1.44–2.44	1.63	1.21–2.19
Current smokers by number of cigarettes smoked daily						
1–10	103	81	1.46	1.041–2.06	1.21	0.83–1.77
11–20	97	64	1.74	1.21–2.49	1.64	1.10–2.43
21–39	40	10	4.29	2.09–8.80	3.51	1.65–7.45
40+	28	5	5.66	2.14–14.95	5.24	1.90–14.42

CI indicates confidence interval; and OR, odds ratio.
*Adjusted for age.
†Adjusted for age, race, education, hypertension, myocardial infarction, angina, diabetes mellitus, and body mass index.

There is evidence for a dose–response relationship between cigarette smoking and risk of stroke in middle-aged and older adults as well; however, the association is less strong.[6] Our finding is consistent with results from prior studies of women and young adults in general.[2,5,7] Our earlier study among women similarly demonstrated a strong dose–response relationship between current cigarette smoking and IS risk.[5] A study of young adults in Iowa demonstrated a dose response between amount of current cigarette smoking and IS risk but did not stratify their findings by sex.[6] These studies demonstrate that smoking amount is an important risk factor for IS but do not characterize the dose–response relationship in young male smokers.

Our study builds on this research by focusing on young men. Our results are in line with the findings of a Swedish study of young men that analyzed smoking history among military recruits ages 18 to 20 years as a predictor of IS before age 45 years.[8] Compared with the Swedish study, a strength of our study is that it includes a more ethnically diverse population and is adjusted for education.

Our study also has several limitations. Because we did not record the use of other tobacco products, we cannot exclude the possibility that concurrent use of these products could have affected our results. Similarly, we did not control for factors such as alcohol consumption and physical activity in our model, which may have resulted in unmeasured or residual confounding of our risk estimates. Another limitation of our study is the case–control design, which allows for the possibility of differential recall bias by case–control status. However, the similar findings in the Swedish study, derived from a cohort design, suggest that there was not a major effect from differential recall bias.

Smoking rates among patients hospitalized for IS have been increasing.[1] The clinical implications of our finding are, that while complete cessation of smoking is the goal, even reducing the number of cigarettes smoked may have beneficial health effects.

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Disclosures

Dr Merino serves as US Research Editor for the British Medical Journal, stroke outcome adjudicator for the Women's Health Initiative, and coeditor of the Blogging Stroke Blog of the Stroke Journal. The other authors report no conflicts.

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