Risk of Stroke and Myocardial Infarction After Reduction or Cessation of Cigarette Smoking

A Cohort Study in Korean Men

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Background and Purpose—The effect of smoking reduction on cardiovascular disease outcomes has not been studied in Asian populations.

Methods—A total of 475 734 Korean men aged 30 to 58 years, stratified into 9 groups based on smoking status at 2 different time points (1990 and 1992), were followed from 1992 to 2001 for the occurrence of stroke or myocardial infarction (MI) events.

Results—Compared with nonreducing heavy smokers (≥20 cigarettes/d), those who quit smoking showed significantly lower risks of ischemic stroke, subarachnoid hemorrhage, and MI with hazard ratios (95% confidence intervals [CI]) of 0.66 (0.55 to 0.79), 0.58 (0.38 to 0.90), and 0.43 (0.34 to 0.53), respectively. For hemorrhagic stroke, quitters showed lower risk compared with heavy smokers, but the difference was not statistically significant (hazard ratio 0.82, 95% CI: 0.64 to 1.06). Compared with nonreducing heavy smokers, the risks of all stroke combined and MI among reducers tended to decrease, although the reductions were not statistically significant. The risks of subarachnoid hemorrhage and MI in those who reduced from moderate to light smoking tended to be lower than in nonreducing moderate (10 to 19 cigarettes/d) smokers. The association between the reduction of smoking level and the risk of stroke and MI did not change significantly when the analysis was limited to those whose smoking status in 1992 was maintained up to 1994.

Conclusions—Smoking cessation was associated with a decrease in the risks of ischemic stroke, subarachnoid hemorrhage, and MI. More studies are needed to verify the likely health benefits of reducing smoking. (***Stroke*. 2008;39:2432-2438.)**

Key Words: smoking ■ stroke ■ myocardial infarction ■ South Korea

Whereas reductions in mortality attributable to cerebrovascular disease and ischemic heart disease (IHD) have been observed in Western countries, these conditions have increased markedly in Asian countries. Stroke is the third most common cause of death and is a leading cause of severe disability in both developed and developing countries.[1] Although IHD incidence is relatively low in South Korea, IHD mortality in Korean men is rapidly increasing (by more than 5- to 6-fold from 1983 to 2004).[2]

Smoking is a well-established risk factor for ischemic stroke, subarachnoid hemorrhage (SAH),[3] and myocardial infarction (MI).[4] However, the relationship between smoking and hemorrhagic stroke is less clear. According to the first systematic review and meta-analysis to consider differential effects of smoking by stroke subtype, smoking increased the risk of ischemic stroke and SAH but paradoxically protected against intracerebral hemorrhage.[5] In a more recent meta-analysis, however, current smokers had a 30% increase in the risk of hemorrhagic stoke.[6]

A recent national survey found that 52.3% of Korean men smoke cigarettes,[7] which is one of the highest rates in the world. Smoking cessation substantially reduces the risk of stroke and coronary heart disease,[8–10] and quitting smoking is an important step toward preventing cardiovascular disease. However, despite the availability of effective treatments for more than two decades, smoking cessation rates remain low.[11] Even in countries with the most effective cessation interventions—tobacco control policies and cessation aids—less than 2% of smokers stop smoking each year.[12] This is likely attributable to the fact that cessation strategies only help a portion of the smoking population to stop smoking, and many smokers either feel unable to quit smoking or do not want to quit.

Harm-reduction strategies are aimed at reducing the adverse health effects of tobacco use in individuals unable or unwilling to quit. Reducing the number of cigarettes smoked per day is one of several kinds of harm reduction strategies.[13] Several intervention studies showed that smoking reduction

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significantly decreased biochemical markers for cardiovascular disease risk.[14–17]

Smoking reduction strategies have various limitations, including a low likelihood of individuals reducing their cigarette smoking, uncertain health benefits from reducing cigarette consumption, and a possible undermining of later smoking cessation by the harm reduction approach.[18]

Recently, several studies have analyzed the ability of smoking reduction to lower health risks. These studies showed no apparent health benefit of smoking reduction for all-cause mortality, fatal and nonfatal MI, and all-cancer mortality, but a small reduction in lung cancer mortality was observed.[19–22] These findings contradict data showing that smoking reduction decreased biological risk factors related to cardiovascular disease.[14–17]

To our knowledge, no study has investigated the effects of smoking reduction on health outcomes outside of northern European countries. Also, no study has considered the effects of smoking reduction on the risks of total stroke and subtypes of stroke. Thus, the objective of this study was to examine the effects of smoking reduction and cessation on the risks of fatal and nonfatal stroke and MI in a cohort of Korean men. Our study population from the Korean National Health Insurance System provides a unique opportunity to evaluate the effect of smoking reduction owing to its large sample size, high prevalence of smoking, and sufficient numbers of stroke and MI events.

Materials and Methods

Study Participants

Study participants were Korean male civil servants aged 30 to 58 years who had available data on their smoking status in two consecutive biennial health examinations (in 1990 and 1992) provided by the Korean National Health Insurance System. Details have previously been published.[23] Females were not included owing to the very low proportion of women civil servants who had ever smoked (0.63% in 1992). Among a total of 518 155 men, 1026 men who had experienced stroke or MI before the beginning of the study, and 13 962 men for whom data on covariates were missing were excluded. In addition, 27 433 men who reported themselves as never smoker or exsmoker in 1990 but were smokers in 1992 were also excluded. Thus, a total of 475 734 men (91.8%) were included in the analysis.

Measurements

Information on smoking status was obtained by completion of a self-administered questionnaire, which included questions with categorical responses on smoking status (ie, never smoked, exsmoker, currently smoking fewer than 10 cigarettes per day, currently smoking between 10 and 19 cigarettes per day, and currently smoking at least 20 cigarettes per day). For our main analyses, we classified study participants into 9 mutually exclusive groups based on smoking status in 1990 and change in smoking status between the baseline examination in 1990 and the follow-up examination in 1992: nonreducing heavy smoker (≥20 cigarettes per day), moderate smoker (10 to 19 cigarettes per day), light smoker (<10 cigarettes per day); reducer from heavy to moderate smoking; reducer from heavy to light smoking; reducer from moderate to light smoking; quitter from any smoking status; sustained exsmoker; and sustained never smoker.

Total cholesterol and fasting glucose levels in venous blood, blood pressure (BP), body weight, height, self-reported alcohol consumption, and engagement in regular physical exercise were assessed during the health examination. Three strata of cholesterol levels were used: <5.16, 5.17 to 6.20, and ≥6.21 mmol/L. Two categories were used for fasting glucose level according to World Health Organization (WHO) criteria: <7.0 and ≥7.0 mmol/L.[24] A single BP measurement was taken by trained nursing staff using a standard mercury or electronic sphygmomanometer. Two categories were used: high BP group, with systolic/diastolic BP of at least 140 mm Hg/90 mm Hg and normal BP group, with systolic/diastolic BP of <140 mm Hg/<90 mm Hg. The weight and height of each patient were measured when the participant was wearing light clothing and no shoes; these data were used to determine body mass index (BMI). BMI, calculated by dividing weight in kilograms by the square of the height (m^2), was categorized into 4 groups according to WHO criteria: <18.5, 18.5 to 24.9, 25 to 29.9, and ≥30 kg/m^2.[25]

The amount of ethanol ingested per week was calculated using drinking frequency per week and the usual amount consumed at each sitting, and estimating ethanol quantity based on the gram weight in the most popular Korean liquor, Soju. Participants were categorized into 4 groups based on weekly alcohol consumption: <30, 30 to 104, 105 to 209, ≥210 g/wk. Participants were also categorized according to whether or not they regularly exercised. We considered socioeconomic position as a potential covariate and so participants were categorized into 4 groups based on a quartile distribution of monthly salary for each age group per year. Area of residence was classified as capital, large city, small city, or rural area, according to the categorization of the administrative jurisdiction.

Outcome Measurement

All strokes and both nonfatal and fatal MIs that occurred between October 1, 1992 and July 31, 2001 were the main outcome events of the study. The following codes in the Tenth Revision of International Classification of Diseases were used to identify and classify the outcomes: MI (I21–I24), all strokes (I60–I69), ischemic stroke (I63, I67.8), hemorrhagic stroke (I61), and SAH (I60). We determined fatal cases through data linkage with death report data from the Korea National Statistical Office. Nonfatal cases were determined through linkage with the medical utilization data of the Korean National Health Insurance System, which provides information on all hospital admissions. Nonfatal events were those cases who were admitted to a hospital for at least 48 hours, to exclude admissions for what turned out not to be a real event. Given the ease with which members of the national health insurance system can access health care data and the obligatory death reporting system in Korea, it is likely that nearly every case was identified.

Analytical Methods

Prospective follow-up started in October 1, 1992 and the participants were censored at the date of admission or date of death attributable to stroke, MI, or other causes; otherwise they were censored at July 31, 2001 if no prior censoring event had occurred. The associations between smoking status and stroke and MI were estimated using Cox proportional hazards regression analysis after testing the proportionality assumption by graphical methods, initially in an age-adjusted model and then in a multivariable-adjusted model. In the analytic model, adjustments were made for conventional cardiovascular risk factors and socioeconomic position. For biological cardiovascular risk factors such as BP, glucose levels, BMI, and cholesterol levels, both the measurement in 1990 and the change between 1990 and 1992 were put in the model as continuous variables. Results are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). To exclude any effect from individuals who might have changed their smoking habit because of health problems, we repeated the multivariable analysis after excluding events that occurred within the first 2 years of follow-up. We also repeated the multivariable analysis in a subgroup (361 066 men, 75.9% of all participants) who reported persistent smoking status up to 1994 to examine the probable bias caused by changes in smoking habits later in follow-up. All analyses were performed using the SAS statistical package (SAS Institute Inc). The Internal Review Board of the Samsung Medical Center approved this study.

Table 1. Change in Smoking Status Between 1990 and 1992

Smoking Status in 1990 (Cigarettes per Day)	Total, n (%)	Nonreducers, n (%)	Reducers to Moderate Smoking, n (%)	Reducers to Light Smoking, n (%)	Quitters, n (%)
Heavy (≥20)	82 365 (27.4)	57 422 (69.7)	15 817 (19.2)	4250 (5.2)	4876 (5.9)
Moderate (10–19)	129 971 (43.2)	100 596 (77.4)	...	18 978 (14.6)	10 397 (8.0)
Light (<10)	88 431 (29.4)	76 004 (86.0)	...	...	12 427 (14.1)
Total	300 767 (100.0)	234 022 (77.8)	15 817 (5.3)	23 228 (7.7)	27 700 (9.2)

Results

Participants were followed for a mean±SD of 8.83±0.95 years between 1992 and 2001, giving a total of 4 202 574 person-years. During this period, there were 6092 stroke events and 2164 MI events.

Table 1 shows changes in smoking status among participants. In 1990, 2 years before the beginning of the study, 63.2% of all participants smoked; 27.4% were heavy smokers, 43.2% were moderate smokers, and the remaining 29.4% were light smokers. During the 2 years before the beginning of the study (between 1990 and 1992), 24.7% of heavy smokers and 14.6% of moderate smokers reduced their level of smoking. During the same period, 5.9% of heavy smokers, 8.0% of moderate smokers, and 14.1% of light smokers stopped smoking.

Table 2 shows baseline characteristics (measured in 1992) and the change in covariates between 1990 and 1992 according to the change in smoking status during this time. Comparisons between nonreducing heavy smokers and individuals who had reduced their smoking levels from heavy to moderate or heavy to light, revealed that reducers tended to be older, have higher BP and blood glucose levels, have lower BMI, and a lower incidence of hypercholesterolemia. They also tended to exercise regularly, consume less alcohol, have lower incomes, and live outside of the capital city.

Table 3 shows associations between change in smoking status and the occurrence of stroke and MI. Compared to nonreducing heavy smokers, quitters had significantly lower rates of ischemic stroke, SAH, and MI, with hazard ratios of 0.66 (0.55 to 0.79), 0.58 (0.38 to 0.90), and 0.43 (0.34 to 0.53), respectively. Quitters also had a lower rate of hemorrhagic stroke compared to nonreducing heavy smokers, but it was not statistically significant (HR 0.82 (0.64 to 1.06)).

The risk of all stroke in heavy smokers who had reduced their smoking levels (reduction from heavy to moderate smoking: HR 0.99 [0.86 to 1.14]; reduction from heavy to light smoking: HR 0.85 [0.68 to 1.06]), or of MI (reduction from heavy to moderate smoking: HR 0.82 [0.65 to 1.03]; reduction from heavy to light smoking: HR 0.92 [0.67 to 1.27]), was lower but was not statistically significant. Moderate smokers who reduced their smoking level had only a slightly lower risk of SAH and MI compared to moderate smokers who had maintained or increased their smoking level. The associations between the reduction of smoking level and the risk of stroke and MI did not change substantially when the analysis was limited to those whose smoking status in 1992 was maintained up to 1994.

Among the nonreducers, compared with heavy smokers, moderate smokers and light smokers had significantly lower risks of ischemic stroke, SAH, and MI in a dose-response pattern, whereas there was no significant association between the level of smoking and the risk of hemorrhagic stroke. Additionally, sustained exsmokers and never smokers had lower risks of all stroke, individual subtype of stroke, and MI compared to heavy smokers.

Discussion

In this large cohort study of Korean male smokers, smoking reduction showed some trends toward risk reduction of all stroke and MI; however, these trends did not reach statistical significance. The lack of significant risk reduction after a reduction in cigarette smoking is in agreement with findings from studies in northern European populations.[19,20,22]

Quitters, exsmokers, and never smokers had significantly lower risks of ischemic stroke, SAH, and MI compared to nonreducing heavy smokers. Further, there were positive associations between the level of smoking and the risks of ischemic stroke, SAH, and MI among nonreducers. These findings are in agreement with previous studies.[8–11] With regard to hemorrhagic stroke, only the sustained exsmokers and never smokers had significant risk reductions compared to heavy smokers, suggesting that a longer duration of smoking cessation is needed to reduce the risk of hemorrhagic stroke.

A lack of association between smoking reduction and risk of ischemic stroke and MI is surprising, given that smoking induces atherosclerosis and the development of MI and ischemic stroke, and that biochemical markers for cardiovascular disease have been shown to be reduced following smoking reduction in intervention studies.[14–17] There are several possible explanations for a lack of association in this study. The first reason could be reverse causality, whereby smoking reduction was a result of health problems. We examined the issue of reverse causality by repeating multivariable analyses with inclusion and exclusion of the events that occurred within the first 2 years of follow-up, and found a small but nonsignificant reduction in the HRs for ischemic stroke, SAH, and MI. This finding seems to support a possible role of reverse causality. Second, reductions in the amount of cigarettes smoked may not necessarily translate into a corresponding reduction in intake levels of toxins contained in cigarette smoke because the smoker may inhale more intensely to maintain nicotine concentrations in the blood.[16] Accordingly, smoking reduction may have a negligible effect on the risk of subsequent cardiovascular events. Third, smoking is correlated with an accelerated progression of coronary atherosclerosis, and with the precipitation of acute cardiovascular events.[26,27] However, smoking is more

Table 2. Characteristics of Study Participants by the Category of Change in Smoking Status Between the Years 1990 and 1992

	Nonreducers			Reducers					
	Heavy Smokers	Moderate Smokers	Light Smokers	Heavy to Moderate	Heavy to Light	Moderate to Light	Quitters	Sustained Exsmokers	Never Smokers
No. of participants	57 422	100 596	76 004	15 817	4250	18 978	27 700	77 368	97 599
Person-years	506 565	889 818	669 566	139 323	36 865	166 299	244 158	684 349	865 631
Age	41.6 (7.5)*	40.9 (7.6)	42.6 (8.4)	41.8 (7.7)	45.8 (8.0)	43.5 (8.5)	42.6 (8.1)	43.9 (8.0)	42.8 (8.2)
Systolic BP in 1990	122.0 (13.2)	122.3 (13.4)	123.0 (14.0)	122.5 (13.6)	124.3 (15.1)	123.4 (14.4)	123.0 (14.3)	124.1 (14.5)	123.9 (14.4)
Change†	0.25 (12.7)	0.04 (12.8)	0.16 (13.1)	0.41 (12.8)	0.73 (13.7)	0.44 (13.4)	0.60 (13.3)	0.46 (13.2)	0.50 (13.0)
Diastolic BP in 1990	79.9 (9.9)	79.9 (10.0)	80.4 (10.3)	80.1 (10.1)	81.4 (10.8)	80.6 (10.5)	80.4 (10.5)	81.3 (10.5)	81.2 (10.5)
Change	0.05 (10.5)	−0.04 (10.5)	−0.02 (10.6)	0.10 (10.5)	0.00 (10.9)	0.05 (10.8)	0.40 (10.8)	0.18 (10.7)	0.23 (10.7)
BMI in 1990	23.4 (2.5)	23.0 (2.4)	23.0 (2.4)	23.2 (2.5)	23.3 (2.5)	23.0 (2.4)	23.2 (2.4)	23.4 (2.4)	23.4 (2.5)
Change	0.14 (1.02)	0.13 (0.98)	0.12 (1.01)	0.11 (1.01)	0.08 (1.07)	0.10 (1.03)	0.37 (1.13)	0.14 (0.98)	0.14 (0.98)
Glucose in 1990	5.00 (1.11)	4.97 (1.00)	5.01 (1.09)	5.00 (1.08)	5.10 (1.21)	5.04 (1.16)	5.01 (1.08)	5.05 (1.09)	5.03 (1.07)
Change	0.09 (1.21)	0.07 (1.14)	0.07 (1.19)	0.08 (1.18)	0.14 (1.32)	0.09 (1.22)	0.11 (1.19)	0.07 (1.16)	0.07 (1.12)
Cholesterol in 1990	4.96 (0.98)	4.86 (0.95)	4.83 (0.96)	4.90 (0.98)	4.96 (0.98)	4.86 (0.97)	4.86 (0.95)	4.90 (0.96)	4.84 (0.95)
Change	0.08 (0.98)	0.08 (0.96)	0.07 (0.97)	0.07 (0.99)	0.07 (1.04)	0.07 (0.97)	0.11 (0.97)	0.06 (0.96)	0.06 (0.94)
High BP‡, %	28.7	28.6	30.5	29.5	34.8	31.3	31.8	34.7	34.1
BMI, %									
<18.5	1.3	1.5	1.6	1.4	1.5	1.6	1.1	1.1	1.3
18.5–24.9	69.8	75.6	76.2	73.4	72.9	76.2	71.2	71.5	71.3
25.0–29.9	27.8	22.2	21.6	24.4	24.8	21.6	26.9	26.7	26.6
≥30.0	1.2	0.7	0.7	0.8	0.8	0.5	0.8	0.7	0.8
Glucose ≥7, %	3.8	3.1	3.5	3.6	5.6	4.2	3.6	3.6	3.3
Cholesterol									
<5.16	58.1	62.4	64.1	60.8	59.4	63.2	61.2	61.6	63.9
5.17–6.19	30.0	27.8	26.5	28.6	28.5	27.2	28.1	28.3	27.0
≥6.20	12.0	9.8	9.4	10.6	12.1	9.7	10.7	10.1	9.1
Regular exercise, %	15.9	20.9	26.7	21.3	28.0	29.1	30.2	35.1	32.5
Ethanol consumption, %									
<30	29.8	28.7	30.7	30.8	39.3	33.5	42.2	43.1	51.1
30–104	17.9	22.3	24.6	21.1	20.9	24.1	23.1	24.4	22.9
105–209	15.5	19.1	19.0	18.4	14.7	18.3	15.0	14.7	12.1
≥210	36.8	29.9	25.7	29.6	25.2	24.1	19.7	17.9	13.9
Pay level (quartile), %									
1st, lowest	24.2	29.3	33.7	28.9	41.4	35.2	27.1	23.2	21.2
2nd	30.4	24.3	24.5	27.0	28.5	25.4	25.7	24.8	23.2
3rd	27.8	27.3	25.0	26.3	18.2	24.1	27.7	30.0	31.3
4th, highest	17.5	19.1	16.9	17.9	11.9	15.4	19.5	22.0	24.4
Area of residence, %									
Capital	19.7	18.0	17.7	19.3	17.1	18.0	20.0	22.7	21.0
Large city	26.8	27.2	27.4	27.9	27.0	27.2	31.2	29.1	28.5
Small city	39.4	40.3	39.6	39.0	38.7	39.5	36.8	36.8	38.0
yOther area	14.1	14.5	15.3	13.9	17.2	15.3	12.1	11.5	12.6

Units for age, BP, BMI, glucose, cholesterol, and ethanol are year, mm Hg, kg/m^2, mmol/L, mmol/L, and g/week, respectively.
*Mean (SD). †Value changed from the year 1990 to 1992. ‡Systolic blood pressure/diastolic blood pressure: ≥140/or ≥90.

strongly associated with a precipitation of acute events than with promotion of the underlying atherosclerosis and even low levels of tobacco consumption can increase the risks of MI and cardiovascular mortality.[28–31] Thus, it may be difficult to clearly demonstrate a beneficial effect of smoking reduction on the risk of cardiovascular events.

Our study included a large sample size, a sufficient number of outcome events, and the availability of information on other major risk factors, which ensured sufficient statistical power to investigate an independent association between the various levels of smoking reduction and stroke subtypes/MI. However, there were some limitations that need to be con-

Table 3. Associations Between the Change in Smoking Status and Cardiovascular Disease

		Nonreducers			Reducers					
	No. of Events	Heavy Smokers	Moderate Smokers	Light Smokers	Heavy to Moderate	Heavy to Light	Moderate to Light	Quitters	Sustained Exsmokers	Never Smokers
All stroke										
Crude incidence*		165	135	166	172	241	191	141	123	1130
Age-adjusted HR†	6092	1	0.86	0.86	1.01	0.95	0.90	0.74	0.58	0.65
			(0.79,0.94)	(0.78,0.94)	(0.87,1.16)	(0.77,1.19)	(0.79,1.03)	(0.65,0.84)	(0.52,0.64)	(0.59,0.71)
Multivariable adjusted HR‡	6092	1	0.86	0.84	0.99	0.85	0.88	0.70	0.53	0.57
			(0.78,0.93)	(0.77,0.93)	(0.86,1.14)	(0.68,1.06)	(0.77,1.00)	(0.62,0.80)	(0.48,0.58)	(0.52,0.63)
Multivariable adjusted HR¶	5062	1	0.87	0.85	0.97	0.91	0.88	0.67	0.52	0.56
			(0.79,0.96)	(0.77,0.93)	(0.83,1.14)	(0.72,1.15)	(0.76,1.01)	(0.58,0.77)	(0.47,0.58)	(0.51,0.62)
Multivariable adjusted HR§	4077	1	0.89	0.87	0.80	1.01	0.93	0.64	0.56	0.58
			(0.79,0.99)	(0.78,0.98)	(0.63,1.02)	(0.65,1.57)	(0.75,1.14)	(0.54,0.77)	(0.50,0.63)	(0.52,0.65)
Ischemic stroke										
Crude incidence		84	65	80	96	129	95	70	57	58
Age-adjusted HR	2958	1	0.82	0.78	1.09	0.94	0.84	0.70	0.50	0.56
			(0.72,0.93)	(0.69,0.89)	(0.90,1.32)	(0.70,1.26)	(0.70,1.01)	(0.58,0.83)	(0.44,0.57)	(0.49,0.63)
Multivariable adjusted HR	2958	1	0.83	0.79	1.10	0.86	0.85	0.66	0.46	0.49
			(0.73,0.94)	(0.70,0.90)	(0.90,1.33)	(0.64,1.16)	(0.70,1.02)	(0.55,0.79)	(0.40,0.53)	(0.43,0.56)
Multivariable adjusted HR	2467	1	0.82	0.79	1.03	0.91	0.81	0.62	0.45	0.48
			(0.72,0.94)	(0.68,0.90)	(0.83,1.28)	(0.66,1.25)	(0.66,0.99)	(0.51,0.75)	(0.39,0.52)	(0.42,0.56)
Multivariable adjusted HR	1966	1	0.86	0.82	0.86	0.88	0.78	0.57	0.49	0.5
			(0.74,1.01)	(0.70,0.96)	(0.62,1.20)	(0.47,1.66)	(0.57,1.07)	(0.44,0.74)	(0.42,0.58)	(0.42,0.58)
Hemorrhagic stroke										
Crude incidence		38	31	41	36	43	45	36	33	39
Age-adjusted HR	1546	1	0.85	0.94	0.91	0.78	0.95	0.84	0.70	0.89
			(0.71,1.03)	(0.78,1.13)	(0.67,1.24)	(0.47,1.29)	(0.73,1.24)	(0.66,1.08)	(0.58,0.84)	(0.75,1.07)
Multivariable adjusted HR	1546	1	0.83	0.91	0.87	0.61	0.90	0.82	0.65	0.79
			(0.69,1.00)	(0.75,1.09)	(0.63,1.18)	(0.36,1.02)	(0.69,1.18)	(0.64,1.06)	(0.53,0.79)	(0.66,0.95)
Multivariable adjusted HR	1193	1	0.91	0.99	0.98	0.63	1.07	0.83	0.70	0.82
			(0.73,1.12)	(0.80,1.23)	(0.69,1.39)	(0.35,1.15)	(0.79,1.44)	(0.62,1.12)	(0.56,0.88)	(0.67,1.02)
Multivariable adjusted HR	1025	1	0.81	0.91	0.81	0.66	1.21	0.75	0.70	0.78
			(0.64,1.03)	(0.72,1.16)	(0.49,1.33)	(0.21,2.09)	(0.81,1.79)	(0.52,1.07)	(0.56,0.89)	(0.62,0.98)
Subarachnoid hemorrhage										
Crude incidence		18	17	14	16	22	19	11	10	10
Age-adjusted HR	577	1	0.99	0.75	0.91	0.96	0.96	0.60	0.48	0.50
			(0.76,1.28)	(0.56,1.00)	(0.58,1.45)	(0.47,1.99)	(0.64,1.43)	(0.39,0.92)	(0.35,0.65)	(0.37,0.67)
Multivariable adjusted HR	577	1	0.96	0.73	0.90	0.96	0.93	0.58	0.44	0.46
			(0.74,1.25)	(0.55,0.98)	(0.57,1.42)	(0.46,1.98)	(0.62,1.40)	(0.38,0.90)	(0.32,0.61)	(0.34,0.62)
Multivariable adjusted HR	474	1	0.99	0.67	0.83	0.99	0.83	0.52	0.44	0.42
			(0.75,1.32)	(0.48,0.92)	(0.50,1.39)	(0.46,2.16)	(0.52,1.32)	(0.32,0.84)	(0.31,0.63)	(0.30,0.59)
Multivariable adjusted HR	411	1	0.98	0.75	0.62	0.53	0.99	0.58	0.43	0.44
			(0.72,1.35)	(0.53,1.07)	(0.28,1.35)	(0.07,3.84)	(0.53,1.85)	(0.33,1.01)	(0.30,0.62)	(0.30,0.63)
Myocardial infarction										
Crude incidence		80	54	57	66	113	66	41	363	30
Age-adjusted HR	2164	1	0.71	0.61	0.79	0.94	0.65	0.44	0.40	0.32
			(0.62,0.81)	(0.53,0.70)	(0.63,0.99)	(0.68,1.29)	(0.53,0.81)	(0.36,0.55)	(0.34,0.46)	(0.28,0.38)
Multivariable adjusted HR	2164	1	0.74	0.65	0.82	0.92	0.69	0.43	0.37	0.29
			(0.65,0.85)	(0.57,0.75)	(0.65,1.03)	(0.67,1.27)	(0.56,0.85)	(0.34,0.53)	(0.32,0.44)	(0.25,0.34)
Multivariable adjusted HR	1786	1	0.75	0.63	0.79	0.80	0.69	0.45	0.36	0.28
			(0.65,0.87)	(0.54,0.74)	(0.61,1.01)	(0.55,1.16)	(0.55,0.87)	(0.36,0.57)	(0.30,0.43)	(0.24,0.34)
Multivariable adjusted HR	1418	1	0.76	0.68	0.86	0.53	0.71	0.39	0.40	0.30
			(0.64,0.90)	(0.57,0.81)	(0.61,1.22)	(0.22,1.29)	(0.50,1.02)	(0.28,0.53)	(0.34,0.48)	(0.25,0.36)

*No. of events/100 000 person-years.

†Adjusted for age using Cox proportional hazard model.

‡Adjusted for age, height, systolic blood pressure, body mass index, fasting total cholesterol, fasting glucose, ethanol consumption, regular exercise, monthly salary level, and area of residence.

||Adjusted for all of the covariates mentioned above and with first 2-years of events excluded.

§Adjusted for all of the covariates mentioned above in a subgroup of participants whose changed smoking habits between 1990 and 1992 were sustained to 1994.

sidered. For example, smoking status can change over time. In a Danish study, only 50% of people who reduced their level of smoking maintained the lower level, 25% quit, and another 25% resumed heavy smoking after 10 years,[20] which could have caused either an under- or overestimation of the effects of smoking reduction. We were unable to measure the change in smoking status up to the occurrence of cardiovascular events. There is a possibility that we would have been able to observe a significant reduction in cardiovascular risk if there were data available from multiple time points up to the time of cardiovascular event. This is because the risk of both MI and SAH was lower for heavy smokers that had reduced to light smoking if the reduction was sustained until 1994 compared to reduction only until 1992.

It is probable that subclinical atherosclerosis was present in subjects at the beginning of the study and that its severity was influenced by the duration and amount of smoking. In this regard, reducing smoking could be more beneficial to those with a short smoking history, who might have less severe disease, than to those with a long history of smoking. However, the association between the reduction of smoking level and the risk of stroke and MI in short-term smokers was not stronger than in longer-term smokers when we did subgroup analyses with participants for whom data regarding smoking duration were available (data not shown).

Residual and unmeasured confounding variables could also affect evaluation of the effect of smoking reduction. In a Danish study, sustained heavy smoking was associated with a worse cardiovascular risk profile than was reduction of smoking.[20] However, overall risk profiles of participants who had reduced smoking were neither better nor worse than those who maintained their level of smoking in the present study. We tried to minimize the effects of confounding variables by adjusting for a range of potential cardiovascular risk factors, such as socioeconomic position, and by testing the impact of changes in covariates between 1990 and 1992 in an analytic model.

Inaccurate diagnosis of stroke and subtype classification might have resulted in misclassification bias. However, another study using the same data source demonstrated that the accuracy of diagnosis of ischemic and hemorrhagic stroke is more than 80%,[32] and we do not expect the diagnostic accuracy to differ according to smoking status categories.

In the present study, each participant's smoking level was assessed using questions with predetermined response categories. Therefore, we were unable to calculate the exact amount of reduction. This might have led us to underestimate the effects of smoking reduction, especially among individuals who reduced from a heavy to a moderate or from a moderate to a light smoking level. However, it is unlikely that this problem biased the results to a significant degree because the risks of all stroke and MI among individuals who reduced from heavy to light smoking levels (reductions of more than 50%) were not different from those among sustained heavy smokers.

Another limitation of this study was that no biological validation of smoking status was performed and overreporting of smoking reduction seems possible, especially considering that the percentage (close to a quarter) of heavy smokers who reportedly reduced their cigarette consumption was relatively large. Thus, the effects of smoking reduction on the risks of stroke and MI might have been underestimated.

In conclusion, smoking cessation was associated with a significant decrease in the risk of ischemic stroke, SAH, and MI in a cohort of Korean males. Further, though not statistically significant, a trend was observed toward a risk reduction with regard to stroke and MI in heavy and moderate smokers who reduced their smoking levels, suggesting a possible benefit of smoking reduction. Future studies to investigate this are warranted.

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Disclosures

None.

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