Yonsei Medical Journal
Vol. 42, No. 2, pp. 155-160, 2001

Effects of Smoking on the Mortality of Lung Cancer in Korean Men

Il Soon Kim[1], Sun Ha Jee[2], Heechoul Ohrr[1], and Sang-Wook Yi[1]

Departments of [1]Preventive Medicine and Public Health, [2]Epidemiology and Disease Control, Graduate School of Health Science and Management, Yonsei University, Seoul, Korea.

Few studies have examined the effects of smoking on the morbidity and mortality of lung cancer in Korean men. In Korea, where the prevalence of smoking is among the highest in the world, the morbidity and mortality of lung cancer are rapidly escalating. The objectives of this study were to prospectively examine the effects of smoking on lung cancer and to determine the combined effects of the amount, duration and age that smoking was started. The design was a prospective cohort study with a follow-up period of six years (1993-1998). The subjects included a total of 305,687 Korean men from 35 to 64 years of age who received health insurance from the Korea Medical Insurance Corporation and who had biennial medical evaluations in 1992. The main outcome measures were deaths from lung cancer. As a baseline, 58.2% were current cigarette smokers. Between 1993 and 1998, 891 lung cancer events (34.4/100,000 people per year) occurred. In multivariate Cox proportional hazards models controlling for age, exercise and alcohol use, current smoking increased the risk of lung cancer (risk ratio [RR], 5.6; 95% confidence interval [CI], 4.2 - 7.3). There were significant dose-response relationships to the amount, duration of smoking and age that smoking was started. Compared with nonsmokers, the RR from current smokers who smoked 20 cigarettes per day for over 30 years was 8.2 (5.9 - 11.3), the RR from current smokers who smoked for over 30 years and were less then 19 years of age when they started smoking was 7.8 (5.2 - 11.9), and the RR for those who smoke 20 cigarettes per day and were less than 19 years of age when they started smoking was 8.3 (5.9 -11.6). This study demonstrates that in Korea smoking is a major independent risk factor for lung cancer, and that the risk increases with an increased amount, longer duration, and younger starting age.

Key Words: Lung cancer, smoking, mortality

Received February 8, 2000
Accepted September 27, 2000

INTRODUCTION

Among Korean adult men, stomach, liver, and lung cancer accounted for over 65% of all deaths from cancer from 1984 to the present. Although stomach cancer contributed the largest number of cancer related deaths, the mortality from stomach cancer has been steadily decreasing over the past 20 years. Since 1980, lung cancer mortality has been reported as the most rapidly increasing cause of death among Koreans. The rate increased from 2.1/100,000 in 1980 to 30.7/100,000 in 1998 among men and from 1.4/100,000 in 1980 to 10.5/100,000 in 1998 among women.[1] This increase in lung cancer mortality has been persistent in men and women despite the fact that few women smoke, while the prevalence of smoking among Korean adult men is 72%.[2] Other risk factors for lung cancer, such as radon and asbestos, are uncommon, so passive smoke was reported as a cause of lung cancer in women.[3]

Cigarette smoking is widely recognized as a major risk factor for lung cancer in Western countries.[4-7] Nonetheless, few studies have examined the relationship between cigarette smoking and lung cancer in Korean men. In this setting, we prospectively examined the effects of smoking on lung cancer and the combined effects of the amount, duration and age at which smoking was started.

MATERIALS AND METHODS

The Korea Medical Insurance Corporation provides health insurance to government employees, teachers and their dependents. Of the entire Korean population, approximately 43 million in 1990, 4,603,361 (11%) were insured by the Korea Medical Insurance Corporation, including 1,213,594 workers and their 3,389,767 dependants. All insured workers are required to participate in biennial medical examinations performed by the Korea Medical Insurance Corporation.[8,9] In 1992, 94% completed the biennial examinations.

The Korean Active and Passive Smoking study is a prospective cohort study designed to assess cigarette smoking for chronic diseases in Korean men and women. Because only 0.6% of the women smoked, we restricted our analysis to men. The study cohort consists of 305,687 men, ages 35-64, who had examinations in 1992. Of the 305,687 men, 5,197 smokers (1.7%) with incomplete data on the amount and/or duration of smoking were excluded. Hence, the final sample size was 300,490.

Data collection

The Korea Medical Insurance Corporation biennial examinations are conducted in a standardized fashion by medical staff at local hospitals. The 1992 biennial medical examination included measurements of weight, height, and serum cholesterol. A fasting blood specimen was drawn and analyzed for total cholesterol. Each hospital that participated in the examination followed internal and external quality control procedures directed by the Korean Association of Laboratory Quality Control. In the 1992 questionnaire, participants were asked to describe their smoking habits, including the number of cigarettes smoked per day and the duration of cigarette smoking in years, along with other health habits including alcohol consumption. The completed questionnaires were reviewed and edited by trained staff.

Using data collected in the 1992 examination, the participants were classified as 'current' smokers if they had smoked currently for at least one year, 'non-smokers' if they never smoked, and 'ex-smokers' if they smoked but had quit. Current smokers were further classified by the average number of cigarettes smoked per day (1-9, 10-19 and 20 cigarettes/day) and duration of smoking (1 - 19, 20 - 29, and 30 years). The body mass index (BMI) was calculated as weight/height^2 (Kg/m^2). The follow-up period lasted six years from January 1993 to December 1998.

The principal outcome variable was mortality from lung cancer. Outcomes were ascertained from the causes of death on the death certificates. In a random sample (N = 100) of lung cancer that occurred in the Korea Medical Insurance Corporation enrollees, we confirmed with a medical chart review that 95.7% of lung cancer diagnoses were definitely correct. In Korea, professionally trained and certified medical chart recorders abstract charts and assign discharge diagnoses in a standardized fashion. Likewise, these recorders complete the death certificates using information provided by the doctors. A computerized search of death certificate data from the National Statistical Office in Korea was performed on each of the Korea Medical Insurance Corporation insured people, so in terms of mortality, the follow-up is likely to be 100% complete.

Statistical analysis

In bivariate analyses, we examined the relationship between smoking status and alcohol consumption, exercise, body mass index and serum cholesterol. In these bivariate analyses, certain trends were tested across the categories of amount of current smoking, using non smokers as the reference. For lung cancer risk factors with a continuous distribution, we used simple linear regression and entered an ordinal variable for the categories of current smoking ('0' for non smokers, '1' for 1-9 cigarettes per day, '2' for 10-19 cigarettes per day, and '3' for 20+ cigarettes per day). We used the method of Mantel Haenszel for the dichotomous variables,[10] excluding ex-smokers in these models.

Cox proportional hazards models were used to assess the independent effects of smoking (both current cigarette smoking and ex-smoking) on lung cancer events, controlling for age, alcohol consumption and exercise. To calculate the population attributable risk (PAR) for cigarette smoking, we used Levins formula.[11] In all analyses, a two-sided alpha level of 0.05 was considered statistically significant.

RESULTS

The mean (SD) age of the study participants was 45.4 (7.4) years. Among the study participants, 174,885 (58.2%) were current smokers and 62,802 (20.9%) were ex-smokers. Among the current smokers, 62% had been smoking for over 20 years, and 27%, 41% and 32% smoked 1-9, 10-19, and 20 cigarettes per day, respectively. The characteristics of non-smokers, ex-smokers and current smokers are presented in Table 1. Smokers were more likely to drink alcohol, while they were less likely to participate in exercise. After adjusting for age, the current smokers consumed significantly more alcohol (p-trend=0.04) and had a lower level of exercise (p-trend=0.01) than the non smokers.

During six years of follow-up (1,682,316 person years), 579 men (2.0%) died from lung cancer. The independent effects of smoking on lung cancer were examined in Cox proportional hazards models that simultaneously controlled for age, alcohol consumption and exercise (Table 2). Compared to non smokers, the risk ratio (RR) for lung cancer was 5.6 for smokers ($p < 0.001$) and 2.4 for ex-smokers ($p < 0.001$). After adjusting for age, alcohol consumption and exercise, the RR for lung cancer was determined for the groups classified by amount of smoking, duration of smoking and age at which smoking was started. The risk of lung cancer increased progressively with higher levels of daily consumption (p-trend < 0.01), increased duration of smoking (p-trends < 0.01) and earlier starting age (p-trends < 0.01).

An examination was made of the combined effects of smoking histories such as duration, amount and age at which smoking was started. Compared with nonsmokers, the RR from current smokers who had smoked 20 cigarettes per day for over 30 years was 8.3 (5.9-11.6), the RR from current smokers who had smoked for over 30 years and were less than 19 years of age when they started smoking was 7.8 (5.2-11.9), and the RR from those who had smoked 20 cigarettes per day and were less than 19 years of age when they started smoking was 8.1 (4.9-13.5). For current smoking, we estimated the population attributable risks for lung cancer, using smoking prevalence estimates from this study. For lung cancer, current smoking accounted for 76.3% of events.

DISCUSSION

In this large, prospective, observational study of Korean men we documented that current cigarette smoking was a strong, independent risk factor for lung cancer. There were significant dose-response relationships, alone and combined, with amount,

Table 1. Baseline Characteristics of 300,490 Men in the Korean Active and Passive Smoking Study, 1992, According to Smoking Status*

Characteristics	Nonsmokers	Ex-smokers	Current smokers, No. of cigarettes per day			
			1-9	10-19	≥20	P for trend
Age (year)	45.9 (7.4)	46.4 (7.6)	45.9 (7.6)	44.7 (7.2)	44.2 (6.9)	.06
Total cholesterol (mg/dl)	192.4 (34.6)	194.4 (34.7)	192.3 (37.4)	194.2 (33.5)	197.5 (35.8)	.34
Body mass index (Kg/m^2)	23.6 (2.5)	23.7 (2.5)	23.2 (2.5)	23.2 (2.5)	23.5 (2.6)	.30
Alcohol consumption, No. of drinks per day	1.8 (3.1)	2.0 (3.0)	2.2 (3.3)	2.4 (3.2)	3.2 (4.2)	.03
Condition (%)						
Hypercholesterolemia[#]	10.0	11.1	10.1	10.6	12.3	.08
Alcohol use[§]	59.6	68.6	80.2	80.9	79.0	.04
Exercise	35.6	37.8	32.7	25.9	18.8	<0.1

*Data are expressed as mean (SD) unless otherwise indicated. All values were age-adjusted (except for age).
[#]Total cholesterol level of at least 240 mg/dl.
[§]Consumption of any alcohol.
[¶]Testing for trend across nonsmokers and current smokers; ex-smokers excluded.

Table 2. Risk of Mortality from Lung Cancer in Korean Men in the Korean Active and Passive Smoking Study*

Variables	Categories	No. of cohort	Incidence of 100,000 P-Y	Risk ratio	95% C.I.
	Nonsmoker	63,713	10.1	1.0	
Smoking status	Ex-smoker	63,955	25.9	2.4	1.8 - 3.3
	Current smoker	178,018	46.3	5.6	4.2 - 7.3
Amount of smoking (cigarettes/day)	1-9	47,584	42.2	4.2	3.1 - 5.7
	10-19	73,843	38.3	4.7	3.5 - 6.3
	20+	56,591	59.9	8.6	6.4 - 11.5
	1-19	86,660	14.4	4.5	3.2 - 6.5
Duration (year)	20-29	71,786	32.4	4.6	3.4 - 6.3
	30+	29,104	144.7	5.8	4.3 - 7.8
	30+	85,447	32.1	3.8	2.9 - 5.1
Age of starting smoking (year)	20-29	102,040	36.1	4.8	3.6 - 6.4
	1-19	19,139	32.8	6.7	4.6 - 9.8
Combined effect	Type I	5,589	110.6	8.3	5.9 - 11.6
	Type II	9,165	181.5	7.8	5.2 - 11.9
	Type III	8,458	35.7	8.1	4.9 - 13.5

*Risk Ratios (RR) and 95% confidence intervals (CIs) from multivariate Cox proportional hazards models adjusting for age, exercise, and alcohol use. P-Y means person-year.
Type I: Combined effect of those who smoked 20 cigarettes per day for over 30 years.
Type II: Combined effect of those who smoked for over 30 years and less than 19 years of age when they started smoking.
Type III: Combined effect of those who smoked 20 cigarettes per day and less than 19 years of age when they started smoking.

duration of smoking and age at which smoking was started. Furthermore, in the context of a high prevalence of cigarette smoking, our data indicate that this risk factor accounts for a substantial fraction of lung cancer events in Korean men (i.e. 76.3% of lung cancer events).

Previous observation studies conducted in East Asian countries and in other countries yielded consistent results. In one of the oldest observational studies conducted in London,[4-6] cigarette smoking was significantly associated with lung cancer mortality. The risk of developing lung cancer increased with the duration of smoking and the number of cigarettes smoked per day. In 1964, the US Surgeon General reported that in comparison with nonsmokers, average male cigarette smokers have approximately a nine- to ten-fold risk of developing lung cancer, and heavy smokers have at least a 20-fold risk.[7] In a Japanese study comparing smokers with nonsmokers, those who smoked 20 cigarettes per day were eight times more likely to develop lung cancer in Japan.[12] In the current study, the risk of lung cancer was five times higher compared to nonsmokers. Finally, in China,[13] where the smoking rate is increasing, smoking did predict the occurrence of lung cancer (RR=6.5). In a 20-year follow-up study on male British doctors,[5] current smokers were 8.3 times more likely to develop lung cancer than nonsmokers. In the same study, the risk of lung cancer among current smokers increased to 14.9 in a 40-year follow-up.[5]

This study also demonstrated that cigarette smoking was a significant risk factor for lung cancer events. In this respect, our data are consistent with the observational data from Japan, China, the United States and the United Kingdom. In the current study, those who smoked 20 cigarettes per day for 30 years were 8.2 times more likely to develop lung cancer than nonsmokers. Thus, the risk is sizable and similar to the results from previous studies.

In terms of the size the effect of smokers versus nonsmokers on lung cancer, our results were relatively smaller than previous studies, including those conducted in the United states and the

United Kingdom. Also, the mortality rate from lung cancer per 100,000 people was 30.7, which is relatively lower than that of the US and UK. This difference between Korea and the US and UK could be explained in several ways. First, the smoking epidemic is relatively recent in Korea (about 20 years since 1980).[15] Deaths from lung cancer are rapidly escalating, but have not yet reached a peak, meaning that death from lung cancer will continuously increase in the near future.[14] In the case of the US[7] and UK,[6] the lung cancer death rate per 100,000 people was approximately 60 in the 1960s. Second, the follow-up period of our study was a mere six years. These characteristics might diminish the size of effect of smoking on lung cancer.

Among the strengths of the this study are high follow-up rates, repeated measures of several exposures (alcohol consumption, total serum cholesterol, weight and height) and its large, national sample. Other aspects of the study population deserve some comments. First, the this study participants tended to be middle-class, employed individuals, who may be healthier than the general population in Korea. Although the incidence rates of disease likely differ by socio-economic status, there is little reason to suspect that risk factor-disease relationships should markedly differ. Second, because smoking remains uncommon among Korean women (just 0.6%),[3] we restricted our analyses to men. Finally, most the Korea Medical Insurance Corporation enrollees were middle-aged, so the patterns of disease may change as the cohort ages change. In particular, the proportionate morbidity and mortality from lung cancer should increase with time.

The potential limitations of our study include the relatively brief duration of follow-up, inclusion of individuals with prevalent lung cancer in the cohort, and reliance on diagnoses from discharge summaries and death certificates. Although the duration of follow-up in our analyses was just six years, the large size of the cohort (> 300,000 participants) provided sufficient statistical power, even in the subgroup and dose-response analyses. The reliance on diagnoses from death certificates may introduce random and systematic errors. A random error would tend to diminish the study's power to detect associations, and a systematic error could alter the distribution of events and perhaps risk factor-disease relationships if the error was related to exposure status. However, the consistency of our findings, i.e. significant relationships of current smoking with lung cancer, suggest that any major systematic errors related to the coding of lung cancer events were unlikely.

In conclusion, current cigarette smoking is a major, independent risk factor for lung cancer in Korea, an East Asian country with a high prevalence of smoking.

Sun Ha Jee, PhD, MHS
Department of Epidemiology and Disease Control, Graduate School of Health Science and Management, Yonsei University, C.P.O. Box 8044, Seoul 120-752, Korea.
Tel: 82-2-361-5095, Fax: 82-2-365-5118,
E-mail: jsunha@yumc.yonsei.ac.kr

REFERENCES

1. National Statistical Office. Annual Report on the Cause of Death Statistics. Republic of Korea, 1996.
2. Gallup Korea. Social and Marketing Trends. In the Korea Gallup Report, 1994. Report No. 12.
3. Jee SH, Ohrr H, Kim IS. Effects of husband's smoking on the incidence of lung cancer in Korean women. Int J Epidemiol 1999;28:824-8.
4. Doll R, Hill AB. The Mortality of Doctors in Relation to their Smoking Habits. A preliminary report. Br Med J 1954;26;1451-5.
5. Doll R, Peto R. Mortality in Relation to Smoking: 20 Years' Observations on Male British Doctors. Br Med J 1976;2:1525-36.
6. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in Relation to Smoking: 40 Years Observations on Male British Doctors. Br Med J 1994;309:901-11.
7. US Department of Health, Education, and Welfare. Smoking and Health. Report of the Advisory Committee to the Surgeon General of the Public Health Service. 1964, USA.
8. Jee SH, Appel LJ, Suh I, Whelton PK, Kim IS. Prevalence of Cardiovascular Risk Factors in South Korean Adults: Results from the Korea Medical Insurance Corporation (KMIC) Study. Ann Epidemiol 1998;8:14-21.
9. Jee SH, Suh I, Kim IS, Appel LJ. Smoking and Atherosclerotic Cardiovascular Disease in Men with Low Levels of Serum Cholesterol. JAMA 1999;282:

2149-55.
10. Breslow NE, Day NE. Statistical Methods in Cancer Research. Vol 1: The Analysis of Case-control Studies. Lyon, France: IARC Scientific Publication; 1980 No. 32. p. 146-50.
11. Levin ML. The Occurrence of Lung Cancer in Man. Acta Unio. Int Contra Cancrum 1953;19:531.
12. Ministry of Health. Smoking and health. Vol 2, 1993. p. 51.
13. Yuan JM, Ross RK, Wang XL, Gao YT, Henderson BE, Yu MC. Morbidity and Mortality in Relation to Cigarette Smoking in Shanghai, China. JAMA 1996;275: 1646-50.
14. Jee SH, Kim IS, Suh I, Shin D, Appel LJ. Projected Mortality from Lung Cancer in South Korea, 1980-2004. Int J Epidemiol 1998;27:365-9.
15. Korean Association of Smoking and Health. Smoking statistics in Korea, 1999.