Retrospective Cohort Study of Smoking and Lung Cancer Incidence in Rural Prefecture, Japan

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Abstract

Objectives: We conducted an epidemiological study of the relationship between lung cancer incidence and smoking, with special reference to the benefits of smoking cessation for reducing lung cancer incidence, to promote a local smoking control program.

Methods: The study was a retrospective cohort study. The population studied was 16,383 male examinees of lung cancer health examinations in 1995 in Tottori Prefecture, Japan. Smoking status from the questionnaire during the health examination was used as the exposure variable. Endpoint (lung cancer incidence) was obtained from the Tottori population-based cancer registry. A multi-variable analysis using the Cox proportional hazard model was adapted for statistical analysis. The average follow-up period was 4.3 years.

Results: The hazard ratio of current smokers for the incidence of lung cancer was 4.9, whereas that of ex-smokers was 2.2. The dose-response relationship between lung cancer incidence and lifetime cigarette consumption (pack year) was determined. The ratio increased among younger subjects (under 65 years old). The hazard ratio of ex-smokers decreased with years just after quitting smoking, and reached the level of never smokers after 10–19 years from smoking cessation.

Conclusions: We reconfirmed that the magnitude of risk estimates of smoking for lung cancer incidence was similar to those of previous studies, and smoking cessation was effective for reducing lung cancer risk.

Key words: cigarette smoking, lung cancer, cohort study, smoking cessation, Japan

Introduction

It has been well established by many epidemiological studies that smoking causes cancers, particularly lung cancer (1). Major organizations and agencies have published reports informing that smoking causes cancers in various parts of the body (2, 3). Comparing epidemiological studies of smoking and cancer between Japan and Western countries, we have observed a lower relative risk in Japanese studies (4). This may be due to the delay of the temporal smoking epidemic pattern or relatively higher incidence rate among nonsmokers in Japan

compared with western countries (4). To evaluate the difference, it is very important to conduct a cohort study of smoking and cancer incidence periodically. Although a considerable number of epidemiologic studies on this issue have been published in Japan, there are few cohort studies adopting lung cancer incidence as an endpoint of the studies (4–7) after the Six Prefecture Cohort Study conducted between 1966 and 1981 (8). Since cancer death was reportedly influenced by access to medical services, development of medical treatment, and health policies on medical services, an epidemiological study adopting cancer incidence as the endpoint of the study is preferable to assessing the association between cancer and risk behaviors. The current study was conducted to determine the recent risk posed by smoking in the development of lung cancer incidence using a retrospective cohort study based on the Tottori cancer registry. The purpose of this study was to assess the association between smoking and lung cancer incidence by linking existing database of the population-based cancer registry to the information obtained from health examination.

Received Aug. 21, 2006/Accepted May 17, 2007

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Methods

Subjects of this cohort study

Tottori Prefecture is located on the western part of Honshu (the main island) and faces the Sea of Japan. The follow-up population of this retrospective cohort study was composed of men who underwent lung cancer examinations in 1995 in Tottori Prefecture. Females were excluded from this study because of their extremely low smoking rate. Although the number of male examinees was 16,487, a total of 16,383 males were enrolled in the study because 104 male examinees already had cancer at the start of the follow-up. The male examinees answered questions including items about smoking status at the beginning of the examination. The factors used in analyses were smoking status, number of cigarettes consumed per day, smoking years, years from quitting smoking and age at quitting smoking.

Detection of endpoint of survey

The incidence of cancer, which is the endpoint of this study, was determined using the population-based cancer registry in Tottori Prefecture. Tottori Prefecture has a population of about 612,000, which is the smallest prefecture population in Japan. The Tottori Prefectural government established the Tottori Prefecture Health Promoting Council in collaboration with the Tottori Medical Association and Tottori University. This council has developed a population-based cancer registry in 1979. The cancer registry has confirmed non-registered cancer cases using death certificates. The Death Certificate Notification (DCN) percentage between 1995 and 1999 was 31.7%.

Linkage of data from health examination to cancer registry was accomplished by using name, address, and data of birth. The examinees were followed-up from 1995 until the end of 1999. The average follow-up period was 4.33 years. The subjects in this study consisted of 15.1% of the male population

over 40 years old of Tottori Prefecture in 1995. The age-adjusted incidence rate of cancer for all sites was 399.7 per 100,000 people for males and 231.4 for females. The incidence rates of lung cancer were 56.0 for males and 18.2 for females (standard population: 1985 Japanese population). These figures are similar to the national average estimates.

Indices on smoking

The examinees were asked to fill in a questionnaire on smoking behavior before health examination. The questions on smoking behavior consisted of smoking status (current smoker, ex-smoker, never smoker), age at the initiation of smoking, and age at the cessation of smoking for ex-smokers. Smoking intensity for current smokers and ex-smokers was evaluated by pack-year, which was defined as the number of years of smoking $\times$ the average number of cigarettes smoked per day/20.

Statistical analyses

The relative risks of current smokers and ex-smokers were calculated by applying the Cox proportional hazard model. When we analyzed the dose-response relationship between lung cancer incidence and pack-year or years after smoking cessation, we divided current or ex-smoker into 4 groups. To compare the risk of smoking in the development of lung cancer between relatively younger subjects (under 65 years old) and older subjects (65 years and over), we conducted statistical analyses separately. The statistical analyses were performed using SPSS (version 12.0) software (SPSS Inc. USA) for Windows. This study was approved by the Ethics Committee of the Faculty of Medicine, Tottori University.

Results

The total person-year of the follow-up population was 70,357, and 904 cancer cases were identified in this study.

Table 1 Hazard ratio of cigarette smoking on cancer incidence

Site	Smoking status	Number of subjects	person-year	incident cases	CIR	Hazard ratio	95% C.I.
All sites	Never smoking	5,322	22,996	242	1052.4	1.0	
	Smoking	7,019	30,100	407	1352.2	1.5	1.3–1.9
	Ex-smoking	4,042	17,261	255	1477.3	1.4	1.2–1.7
	total	16,383	70,357	904	1284.9		
Stomach	Never smoking	5,322	22,996	73	317.4	1.0	
	Smoking	7,019	30,100	120	398.7	1.4	1.1–1.9
	Ex-smoking	4,042	17,261	72	417.1	1.3	0.9–1.8
	total	16,383	70,357	265	376.7		
Colon	Never smoking	5,322	22,996	36	156.5	1.0	
	Smoking	7,019	30,100	49	162.8	1.2	0.8–1.8
	Ex-smoking	4,042	17,261	48	278.1	1.8	1.1–2.7
	total	16,383	70,357	133	189.0		
Lung	Never smoking	5,322	22,996	16	69.6	1.0	
	Smoking	7,019	30,100	77	255.8	4.9	2.8–8.4
	Ex-smoking	4,042	17,261	26	150.6	2.2	1.2–4.1
	total	16,383	70,357	119	169.1		
Esophagus	Never smoking	5,322	22,996	7	30.4	1.0	
	Smoking	7,019	30,100	21	69.8	2.6	1.1–6.3
	Ex-smoking	4,042	17,261	10	57.9	1.9	0.7–4.9
	total	16,383	70,357	38	54.0		

Adjusted by age.

Age-specific cancer incidence increased with age. The cancer incidence of the 40's age group was 123/100,000 person-year, whereas the cancer incidences of the 50's, 60's, 70's and 80's or over age groups were 508, 1,043, 1,276, and 1,154, respectively. The cancer incidences of the 40's and 50's age groups were similar to those of nationwide estimates, whereas the cancer incidences among the 60's, 70's, and 80's or over age groups of this study population were lower than those of the nationwide estimate (9). The current smoking or ex-smoking was identified as a risk factor for cancer development for stomach, colon, lung, and esophagus cancer by statistical testing

(Table 1). The hazard ratio of smoking to lung cancer was 4.9, whereas that of ex-smokers was 2.2. For lung cancer, a dose-response relationship between the consumption of cigarettes (pack-year) and hazard ratios was observed, and the relationship was also observed among ex-smokers (Table 2).

To determine the effectiveness of quitting smoking, we calculated the hazard ratios of smoking to lung cancer by the number of years from quitting smoking. The hazard ratio of smoking decreased with years from quitting smoking, and almost reached the level of never smokers 10–19 years from smoking cessation. When the hazard ratios of quitting smoking

Table 2 Lifetime cigarette consumption and years after smoking cessation and lung cancer incidence

Categories	Number of subjects	person-year	incident cases	CIR	Hazard ratio	95% C.I.
Risk posed by lifetime cigarette consumption in lung cancer development (excluding ex-smokers)						
never smoker	5322	22996	16	69.6	1.0	
<20 pack-year	995	4303	7	162.7	2.4	1.0–6.0
20–39 pack-year	3115	13379	24	179.4	2.7	1.4–5.1
40–59 pack-year	2291	9769	36	368.5	5.4	3.0–9.8
60 pack-year and over	618	2651	10	377.2	5.6	2.5–12.3
p for trend					0.00	
Risk posed by lifetime cigarette consumption before smoking cessation in lung cancer development (among ex-smokers)						
never smoker	5322	22996	16	69.6	1.0	
<20 pack-year	1379	5909	4	67.7	1.0	0.3–2.9
20–39 pack-year	1439	6168	8	129.7	1.9	0.8–4.3
40–59 pack-year	788	3341	9	269.4	3.9	1.7–8.7
60 pack-year and over	436	1842	5	271.4	3.8	1.4–10.5
p for trend					0.01	
Risk posed by number of years after quitting smoking in lung cancer development (using different reference groups)						
never smoker	5322	22996	16	69.6	1.0	
Less than 5 years	812	3496	6	171.6	2.8	1.1–7.1
5–9 years	673	2870	7	243.9	3.9	1.6–9.4
10–19 years	1330	5653	7	123.8	1.9	0.8–4.6
20 years and over	1205	5147	6	116.6	1.4	0.6–3.6
p for trend					0.00	
current smoker	7019	30100	77	255.8	1.0	
Less than 5 years	812	3496	6	171.6	0.6	0.2–1.3
5–9 years	673	2870	7	243.9	0.8	0.4–1.7
10–19 years	1330	5653	7	123.8	0.4	0.2–0.8
20 years and over	1205	5147	6	116.6	0.3	0.1–0.6
p for trend					0.00	
Risks posed by lifetime cigarette consumption in lung cancer development in subjects under 65 years of age (excluding ex-smokers)						
never smoker	2269	9938	2	20.1	1.0	
Less than 20 pack-year	584	2543	2	78.6	6.3	0.9–44.6
20–39 pack-year	1721	7488	7	93.5	6.8	1.4–32.7
40–59 pack-year	1041	4489	7	155.9	6.9	1.4–33.2
60 pack-year and over	331	1423	2	140.5	6.1	0.9–43.0
p for trend					0.01	
Risks posed by lifetime cigarette consumption in lung cancer development in subjects 65 years and over (excluding ex-smokers)						
never smoker	3053	13058	14	107.2	1.0	
Less than 20 pack-year	441	1760	5	284.1	2.7	1.0–7.4
20–39 pack-year	1394	5891	17	288.6	2.7	1.3–5.5
40–59 pack-year	1250	5280	29	549.2	5.2	2.7–9.8
60 pack-year and over	287	1228	8	651.5	6.1	2.6–14.6
p for trend					0.00	

pack-year: daily consumption (1 unit=20 cigarettes)×years of smoking.

CIR: crude incidence rate (per 100,000 person-year).

Adjusted by age.

to lung cancer were calculated using the current smokers as the reference group, the hazard ratio of quitting smoking decreased just after quitting smoking (Table 2). When the data was limited to persons under 65 years of age, the value of hazard ratio of current smoking to lung cancer increased among smokers with a relatively low level of cigarette consumption (Table 2).

Discussion

Using the data from the population-based cancer registry, we were able to calculate the risk of smoking to lung cancer incidence. We confirmed that cigarette smoking is an important risk factor for developing lung cancer with a dose-response relationship. For ex-smokers, smoking was still a risk factor. As cigarette consumption (number of pack-year) increases, the hazard ratio of smoking for developing lung cancer increases. We also found that smoking cessation decreased lung cancer incidence.

Comparing the results of this study with those obtained by previous studies, our hazard ratios of ex-smoking and smoking on lung cancer incidence were similar to published results from surveys conducted in Japan (4, 10) and Asian countries (11–14) except for Singapore (15), whereas the ratios were lower than these of North America and Western European countries (16–24). It is considered that the relatively low hazard ratio of smoking to lung cancer incidence in Japan is due to the relatively smaller number of cigarettes smoked by smokers, the relatively higher incidence of lung cancer among nonsmokers by passive smoking, the possible preventive effects of Japanese diet, the differences in the histological types of cancer, and genetic susceptibility (4). According to recent studies, the magnitude of risk ratio from cohort studies is slightly higher than that from case-control studies (4). The magnitude of risk ratio from studies of lung cancer incidence was similar to that from studies of lung cancer death (4). Our hazard ratio was similar to that from studies conducted during the 1980s in Japan (8). The results of this study suggest that the health hazard of smoking is consistent with scientific evidence and the magnitude of the hazard ratio has not changed over several decades. This study showed a dose-response relationship between cigarette consumption and lung cancer risk. Most studies determined the relationship using daily cigarette consumption. Although we failed to confirm the relationship between daily cigarette consumption and lung cancer risk, we found a dose-response relationship using the pack-year as a lifetime exposure indicator. This result may demonstrate that pack-year is a better indicator of lifetime smoke exposure predisposing cancer development.

This study also showed the effectiveness of smoking

cessation for decreasing the risk of developing lung cancer. There have been few studies of decreased risk of lung cancer after smoking cessation in Japan (25–27). Since one study was a case-control study and others were cohort studies of the endpoint of cancer death, our study has the advantages of both study design being a cohort study and applied study's endpoint (lung cancer incidence).

There are some methodological problems in this study. First, insufficient follow-up of the cohort population caused by transferring to another prefecture may introduce selection bias into this study. However, the number of persons of moving to another prefecture was small (the proportion of the number of persons over 40 years of age transferring was 0.8% and that of persons 65 years or over transferring was 0.3% in the age-specific prefecture population in 1999) (28). Therefore, the effect of failure of follow-up on the results of this study may be small. Second, since cancer incidence among the elderly population of this study was lower than that of the national estimate, the recipients of health examination are considered as health-conscious persons with a better lifestyle. This selection bias will cause the hazard ratio to become null. Therefore, since we found significant results in these study subjects, these problems have little effect on the interpretation of the study results. Moreover, since a previous study showed that even if other possible risk factors, such as dietary factors, alcohol use, and occupational history among others, were taken into account, all these variables had only little effect on risk estimates for smoking variables (4): insufficient information on possible confounding lifestyle-related factors in this study may not introduce serious problems.

We reconfirmed that the magnitude of risk estimates of smoking for lung cancer incidence was similar to those of previous studies, and that smoking cessation was effective for reducing lung cancer risk. Consequently, the results of this study will provide useful information for health education in this prefecture to prevent and stop smoking.

Acknowledgment

This study was supported by the health and labour science research grants from Ministry of Health, Labour and Welfare in 2000. We would like to thank the Tottori Prefecture Health Promoting Council (Chairperson Akio Nagata, M.D.) for providing cancer incidence data, and we also express our gratitude to all physicians in Tottori Prefecture for cooperating with cancer registration, and to the Tottori Health Service Association and the municipalities of Tottori Prefecture for providing the health examination data.

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