J Korean Med Sci 2007; 22: 524-8
ISSN 1011-8934

Temporal Changes of Lung Cancer Mortality in Korea

The lung cancer mortality in Korea has increased remarkably during the last 20 yr, and, it has become the first leading cause of cancer-related deaths since 2000. The aim of the current study was to examine time trends of lung cancer mortality during the period 1984-2003 in Korea, assessing the effects of age, period, and birth cohort. Data on the annual number of deaths due to lung cancer and on population statistics from 1984 to 2003 were obtained from the Korea National Statistical Office. A log-linear Poisson age-period-cohort model was used to estimate the effects of age, period, and birth cohort. The both trends of male and female lung cancer mortality were both explained by age-period-cohort models. The risks of lung cancer mortalities for both genders were shown to decline in recent birth cohorts. The decreasing trends begin with the 1939 birth cohort for men and 1959 for women. The mortality pattern of lung cancer was dominantly explained by a birth cohort effect, possibly related with the change in smoking pattern, for both men and women. Finally, the mortality of lung cancer in Korea is expected to further increase in both men and women for a while.

Key Words : *Cohort Effect; Lung Neoplasms; Mortality; Korea; Smoking; Linear Models*

Yunhee Choi*, Yeonju Kim*, Yun-Chul Hong*, Sue Kyung Park*, Keun-Young Yoo*,†

Department of Preventive Medicine*, Seoul National University College of Medicine, Seoul; National Cancer Center Research Institute†, Goyang, Korea

Received : 12 June 2006
Accepted : 7 November 2006

Address for correspondence
Keun-Young Yoo, M.D.
Department of Preventive Medicine, Seoul National University College of Medicine, 28 Yeongeon-dong, Jongno-gu, Seoul 110-799, Korea
Tel : +82.2-740-8324, Fax : +82.2-3673-3540
E-mail : kyyoo@plaza.snu.ac.kr

INTRODUCTION

Cancer has been the first leading cause of deaths since 1980s in Korea. The cancer-related mortality has increased from 72 per 100,000 in 1983 to 133.1 per 100,000 in 2003 (1). Four leading sites of cancer mortality in Korea are lung, stomach, liver, and colo-rectum (1). Among them, the lung cancer mortality increased most remarkably, which was from 8.2 and 3.4 per 100,000 in 1983 to 38.6 and 14.0 per 100,000 in 2003 for men and women, respectively. Finally, it has become the first leading cause of cancer-related deaths since 2000. According to a recent report by the Korean National Cancer Center, the lung cancer incidence ranked the second for men and the fifth for women as a common malignant cancer in Korea with the crude incidence rates being 42.1 and 15.1 per 100,000 during 1999-2001 for male and female, respectively.

It is well known that cigarette smoking plays a dominant role in developing lung cancer, being responsible for up to 90 percent of the lung cancer epidemic, not only directly but also in association with other substances such as asbestos and radon (2). Smoking patterns have changed markedly and in different directions over the past decades, and thus the increasing trends in lung cancer mortality differ according to birth cohorts and sexes.

The aim of the current study was to examine time trends of lung cancer mortality during the period 1984-2003 in Korea, assessing the effects of age, period and birth cohort.

MATERIAL AND METHODS

Data on the annual number of deaths due to lung cancer and on population statistics from 1984 to 2003 were obtained from the Korea National Statistical Office (1). Based on these data, the age-specific mortality by sex was calculated for twelve 5-yr age groups (20-24 to 75-79 yr) and four 5-yr calendar periods (1984-1988 to 1999-2003) (Table 1). Using the age and calendar period classification, 15 overlapping 10-yr birth cohorts were identified and defined according to the central year of a birth cohort.

To evaluate the effects of age, period, and birth cohort on lung cancer mortality, log-linear models were fitted by maximum likelihood using the SAS 8.1 (3) and Fortran 90 program. Lung cancer mortality were assumed to follow Poisson distribution. Each factor in models had an additive effect on the log rate as follows,

$$\log \lambda_{ijk} = \mu + \alpha_i + \pi_j + \gamma_k + \varepsilon_{ijk}$$

Where the age effects are represented by α_i, i=1,2,K,10, the period effects by π_j, j=1,K,4, and the birth cohort effects by γ_k, k=1,K,12 (4). The term ε_{ijk} represents random error. A sequence of models was constructed by the one-factor age model, then 2-factor age-drift, age-period, age-cohort models, and finally the age-period-cohort model. The drift term represented a temporal change in mortality not identifiable as a period or birth cohort effect. From the paper by Clayton

(5), the age-drift model should always be considered next to the one-factor age model, and it is only when the drift term does not explain the temporal variation that we must consider a age-period or age-cohort model. Hence, if the age-drift model describes well enough the trend of lung cancer mortality in terms of the measure of goodness of fit, the period or cohort effect will not be estimated, and the lung cancer mortality will be described by a regular time trend, 'drift'. The deviances of the models were compared to test the statistical significance of each factor. Any goodness of fit statistics in models with more than 2 factors was not rejected. Hence, it was unnecessary to estimate an over-dispersion parameter in our analysis. Since age is such an important predictor of the lung cancer mortality, a goodness of fit considering age will be more valuable. Therefore, adjusted R^2_A was computed (6).

In an analysis of age-period-cohort models, a fundamental problem is the linear dependence between age, period, and birth cohort effect, which makes it impossible to disentangle the linear effects of all three terms (non-identifiability problem). To overcome this, the estimable function by Holford (4) was employed to evaluate an age, period, and birth cohort effect. First, we estimated nonlinear effects (or deviations from linearity), which can be uniquely defined (4). The log of relative risks of the nonlinear effects by birth cohort and calendar year were calculated using year of death 1999-2003 and year of birth 1970-1979 as baseline levels, respectively. If the birth cohort effects were significant after adjusting the age and period effect, then the cohort effects were estimated. Here, due to the non-identifiability problem, we need to assume the zero linear period effect to determine the linear cohort effects. Finally, the cohort effects were estimated by the sum of the linear cohort effect and nonlinear cohort effects.

Table 1. Lung cancer mortality per 100,000 by age group for years of deaths

Sex	Age group	Calendar year			
		1984-1988	1989-1993	1994-1998	1999-2003
Male	20-24	0.52	0.49	0.27	0.26
	25-29	1.11	0.70	0.54	0.57
	30-34	1.63	1.58	1.36	1.36
	35-39	3.26	3.88	3.58	2.73
	40-44	7.64	9.11	8.36	6.74
	45-49	18.23	21.74	19.05	16.79
	50-54	34.01	44.58	44.14	38.09
	55-59	65.10	86.55	95.88	81.77
	60-64	98.25	152.98	169.20	165.68
	65-69	129.31	214.30	284.40	276.07
	70-74	127.89	256.60	376.53	430.86
	75-79	130.15	246.46	425.86	566.36
Female	20-24	0.58	0.52	0.28	0.26
	25-29	0.73	0.87	0.44	0.50
	30-34	1.39	1.28	1.07	1.04
	35-39	2.08	2.15	2.36	1.99
	40-44	3.74	4.07	4.24	4.40
	45-49	5.75	7.19	7.08	6.50
	50-54	8.98	11.64	13.32	10.82
	55-59	13.65	18.07	20.85	19.27
	60-64	20.45	27.77	31.61	32.88
	65-69	26.15	44.49	54.82	53.41
	70-74	31.91	55.07	83.75	88.51
	75-79	31.91	63.83	106.24	134.55

RESULTS

Descriptive analysis

The standardized lung cancer mortality in Korea between 1984 and 2003 are shown in Fig. 1. The rates for men increased from 17.6 per 100,000 in 1984 to 51.7 in 2003, almost tripled during the 20 yr. Those for women also have been gradually increased from 4.6 per 100,000 in 1984 to 12.9 in 2003. Fig. 2 shows the trend of age-specific mortality due to lung cancer by birth cohort. The age-specific curves are going downward as age decreases in both sexes. The age-specific mortality of lung cancer increases by birth cohort for age groups older than 60 yr, while it decreases by birth cohort for those younger than 35 yr. The age-specific mortality curves for the other age groups showed a parabolic pattern.

The age-period-cohort analysis

Table 2 shows the goodness of fit (scaled deviance) for the age-period-cohort models. The lung cancer mortality has a different pattern by age and sex, and the age-period-cohort model was fitted separately by sex. First, we considered the drift term. However, the adj-R^2_As for the age-drift models for males and females were 0.47 and 0.54, i.e. the drift term explained only 47% and 54% of male and female lung cancer mortality, respectively. They were much lower than those for the age-cohort or age-period-cohort model, thus we excluded them from the possible models for the pattern of lung cancer mortality. For women, both period and birth cohort

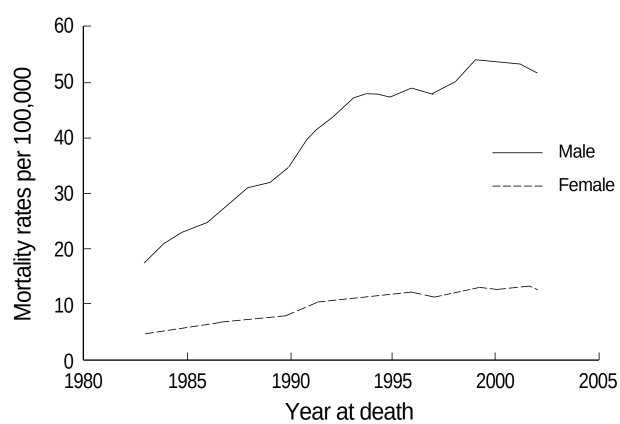

Fig. 1. Age-standardized mortality of lung cancer in Korea, 1984-2003.

Table 2. Summary statistics for age-period-cohort models of lung cancer mortality, year 1984-2003, aged 20-79

Sex	Model	DEVIANCE (df)	ΔD	Δdf	*p*-value	Effect	Adj-R_A^2
Male	AGE (A)	652.3275 (36)					
	AGE+drift (AD)	180.5974 (35)	471.7301	1	<.0001	DIA	0.72
	AGE+PERIOD (AP)	133.5340 (33)	518.7935	3	<.0001	PIA	0.78
	AGE+COHORT (AC)	17.7001 (22)	634.6274	14	<.0001	CIA	0.96
	AGE+P+C (APC)	0.7428 (20)	16.9573	2	0.0002	PIAC	0.998
			132.7912	13	<.0001	CIAP	
Female	AGE	133.3487 (36)					
	AGE+drift	37.7853 (35)	95.5634	1	<.0001	DIA	0.71
	AGE+PERIOD	27.7334 (33)	105.6153	3	<.0001	PIA	0.77
	AGE+COHORT	4.0433 (22)	129.3054	14	<.0001	CIA	0.95
	AGE+P+C	0.3990 (20)	3.6443	2	0.16	PIAC	0.99
			27.3344	13	0.01	CIAP	

DIA, A vs. AD; PIA, A vs. AP; CIA, A vs. AC; PIAC, AC vs. APC; CIAP, AP vs. APC.

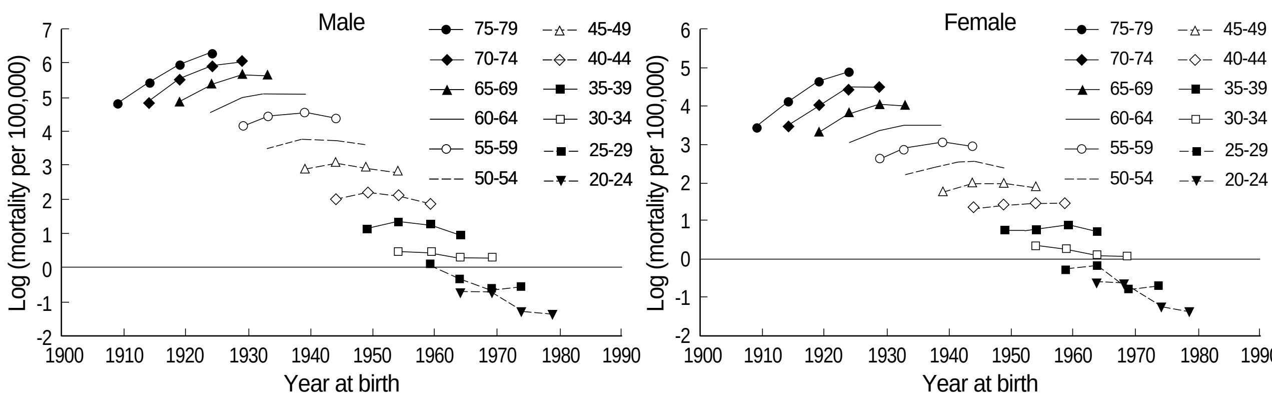

Fig. 2. Age-specific mortalities of lung cancer by year of birth, 1909-1979.

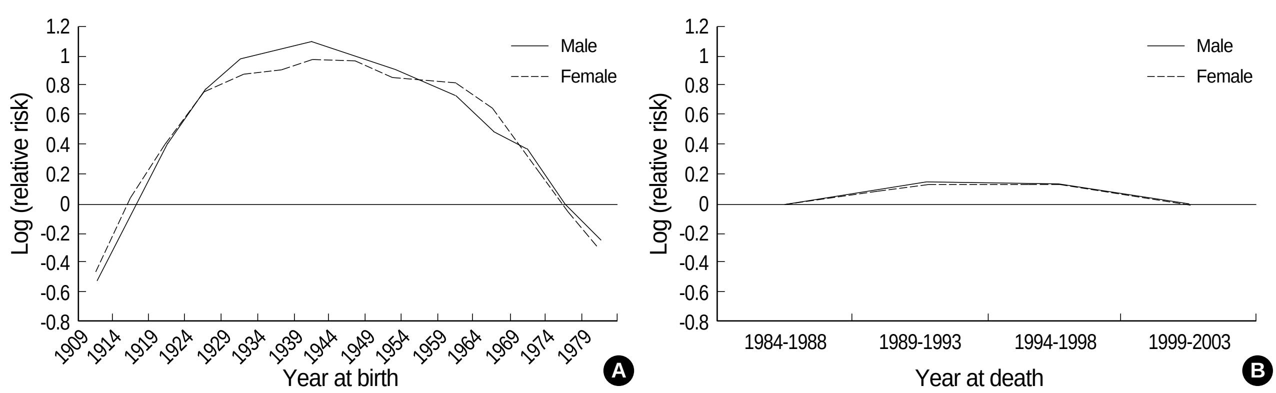

Fig. 3. Nonlinear effects of birth cohort (A) and period (B) on male lung cancer mortality in Korea.

effect were statistically significant ($p<0.001$) after adjusting age. The addition of the birth cohort effect to an age-period model and the period effect to an age-cohort model were significant ($p<0.001$). Therefore, we concluded that the trend of female lung cancer mortality was better represented by the age-period-cohort model. For men, all factors in the age-period-cohort model were statistically significant after adjusting each other. Furthermore, the adj-R_A^2 values were 0.56, 0.90 and 0.99 for the age-period, age-cohort, and age-period-cohort model, respectively. It suggests that the full model is preferred over the 2-factor models.

Fig. 3 shows the nonlinear effects of period and birth cohort for lung cancer mortality. The relative risks by the birth cohorts increased by 1939 birth cohort and steadily decreased thereafter in both men and women. The maximum relative risk by the period effect occurred during 1989-1993 for a male and 1994-1998 for a female. Even if the calendar period was a statistically significant factor after adjusting age and cohort effect, Fig. 3 suggested that its effects were limited compared with the cohort effects. Therefore, the cohort effects

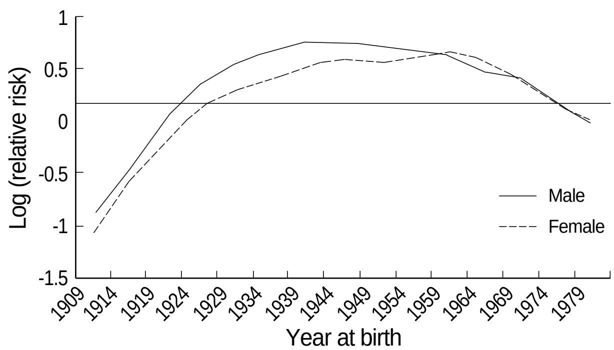

Fig. 4. Cohort effects on lung cancer mortality in Korea.

for lung cancer mortality were estimated under the assumption of zero linear period effect. Plots of the birth cohort effects for each sex are shown in Fig. 4. The curves for cohort effects for both genders have parabolic patterns. The risk of lung cancer mortality increased up to the 1939 birth cohort for males and up to the 1959 birth cohort for females. After that, it steadily decreased for both males and females.

DISCUSSION

The age-period-cohort model analysis in this study revealed that the increasing trends of lung cancer mortality were dominantly explained by the birth cohort effect for both genders. The trends of birth cohort effects from both genders seem to be almost similar: if the cohort effects were estimated in the way their sum went to zero, the effects for the generations born between 1929 and 1969 turned positive, implying higher risk than birth cohorts born before or after this period.

The relationship between cigarette smoking and increased risk of lung cancer has been demonstrated by a large number of case-control studies and cohort studies (7-9). Thus, recent changes in mortality due to lung cancer can be mainly explained by change in smoking patterns over the past decades. Korea has the unique features of a relatively homogeneous ethnic society with a high smoking rate among men and a contrastingly low smoking rate among women. According to the health data by OECD (2003), the prevalence of smoking in Korean adult males in 2001 is 61.8 percent, which is among the highest in the world, whereas the prevalence of smoking in Korean adult female in the same year is quite low at 5.4 percent (10). The prevalence of smoking (over 20 yr of age) in male and female decreased from 79.3 percent and 12.6 percent in 1980 to 56.7 percent and 3.5 percent in 2003, respectively (10).

In addition, lung cancer mortality is linked to the sales of cigarettes approximately 18 to 23 yr earlier (11). In a Korean study, it was also shown that lung cancer mortality reflected patterns of cigarette smoking 20-30 yr ago (12). In Korea, cigarettes were first introduced in 1600s (8). The consumption began to increase with mass production in 1970s, and the increase was accelerated for a while with foreign cigarettes flowing into the domestic market in 1988. Such a continuous increase reached its peak around the early in 1990, and then the consumption remained almost constant in recent years (7). Considering the year of the peak consumption of cigarettes, lung cancer mortality will be maximized in the years between 2015 and 2025. Our analysis provided the consistent results. That is, the risk of death due to lung cancer reached the peak in the 1939 birth cohort in male, and the people in the 1939 birth cohort will be around 80s in the years of 2015-2025. It implies that the lung cancer mortality in male will begin to decrease gradually in all age groups from the year of 2015-2025 because that period is when the most risky generation, the1939 birth cohort, will almost disappear. Note that lung cancer in Korea has occurred predominantly in male smokers (13), and also the smoking rate is high among men and contrastingly low among women. Therefore, not only lung cancer deaths in male but also total lung cancer deaths in Korea will be maximized in the years between 2015 and 2025, as expected.

As shown in Fig. 1, the increase in lung cancer mortality is continuous in women as well as men. The reasons for the increasing pattern in female may be the increase of tobacco consumption among females or passive smoking. However, considering that about one out of four Korean women with lung cancer smoke cigarettes (13), the female smoking pattern does not appear to fully explain the female mortality due to lung cancer. There are several case-control and cohort studies related with lung cancer in non-smokers, mainly women. The high lung cancer incidence in Chinese and Taiwanese women, most of whom are lifetime non-smokers, was explained by exposure to cooking fuels or other indoor air pollutants (14, 15). Also, some studies provided the test of relationship between household passive smoking in early life and lung cancer risk, giving significant results (16-18). A Korean study explained the reason for escalating lung cancer in non-smoker Korean women by their husbands' smoking (12). Hence, Korean women may be likewise exposed to indoor air pollutants such as environmental tobacco smoke from household and work place, and it may play an important role in the development of lung cancer in Korean women. As mentioned earlier, the trends of birth cohort effects from both genders were almost similar. Such a similar pattern seems to imply that female lung cancer mortality can be explained by the change in the smoking pattern as in male, suggesting secondhand smoking as an important risk factor. Therefore, we can hypothesize that the decreasing trend in female lung cancer mortality since the 1959 birth cohort might be related with change in exposure to environmental tobacco smoke due to the reduction in the prevalence of smoking men in Korea.

There are a few studies describing the association between genetic polymorphisms and lung cancer to involuntary smoking have in women. Full gene names should be given genes has been hypothesized to be related with involuntary smoking and lung cancer in non-smoking women. The results are conflicting between ethnicities: a slight positive effect of GSTM1 null type was shown in Japanese non-smoking women but not in Europe, assuming that genetic polymorphisms could contribute to individual susceptibility to develop lung cancer among involuntary smoking women (19).

Even though the lung cancer mortality is mainly explained by the age and cohort effects, there might be a minor but definite period effect because of classification, improved death certification or the survival rate. The classification of the lung cancer did not change during the study period. The proportion of death certificates issued by physicians increased from 44.6% in 1990 to 77.6% in 2002 (20). The improved death certificate may have functioned to increase the lung cancer mortality. On the other hand, screening for early lung cancer detection using various methods has been performed over many years, but there is no good evidence that screening for lung cancer using chest radiography or sputum cytology can reduce the lung cancer mortality (21). In any circumstance, screening methods may function to decrease the lung cancer mortality, and it does not explain the increasing trend in the last 20 yr.

In summary, there was an overall increase in the lung cancer mortality during 1984-2003 in Korea. The mortality pattern of lung cancer was dominantly explained by the birth cohort effect, probably related with change in smoking pattern, for both men and women. Finally, the mortality of lung cancer in Korea is expected to further increase in both men and women for a while, and then stabilization is expected, if other conditions remain unchanged and the previous trend will continue.

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