Original Article

Lung Cancer Epidemiology in Korea

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Purpose

The current study was undertaken to examine the trends in the lung cancer incidence, mortality, and survival after a diagnosis in Korea.

Materials and Methods

Lung cancer incidence data according to the histologic type and mortality data were obtained from the Korea Central Cancer Registry and the Statistics Korea, respectively. The age-standardized incidence and mortality rates were calculated, and the Joinpoint model and age-period-cohort analyses were used to describe the trends in the rates. The 5-year relative survival rates of lung cancer were also calculated.

Results

Although the number of new lung cancer cases increased between 1999 and 2012, the age-standardized incidence rate decreased by 0.9% per year in men, whereas the incidence in women increased by 1.7% per year over the same time. Until 2010, the most common histologic type in men was squamous cell carcinoma, then adenocarcinoma prevailed thereafter. Since 1999, the most frequent histological type in women was adenocarcinoma. The lung cancer mortality started to decrease in 2002, with a more apparent decline for the younger age groups in both men and women. Overall, the 5-year relative survival rates have improved significantly from 11.2% for men and 14.7% for women among patients diagnosed between 1993 and 1997 to 19.3% for men and 28.2% for women among patients diagnosed between 2008 and 2012, respectively. An improvement in survival rate was observed for all major histology groups.

Conclusion

The epidemiology of lung cancer in Korea has changed over a short time span, with decreasing mortality and improving survival rates. Further study is warranted to determine the cause of these changes.

Key words

Lung neoplasms, Epidemiology, Incidence, Mortality, Survival, Adenocarcinoma

Introduction

Lung cancer has been the most common cancer in both incidence and mortality worldwide [1]. However, a decrease in lung cancer incidence and mortality has been observed in men in many developed countries, whereas an increase or no significant changes have been observed in women. When the histological types of lung cancer are considered, the incidence of squamous cell carcinoma and small cell carcinomas has been decreasing, whereas the incidence of adenocarcinomas has been increasing in both men and women [2-5]. This may be explained by changes in the prevalence of tobacco smoking, which is the most important risk factor for lung cancer and accounts for 70%-90% of the lung cancer burden [6,7]. The strongest association between smoking and lung cancer is observed for squamous cell carcinoma and small cell carcinomas (odds ratio, 63 to 111 for smokers > 30 ciga-

rettes/day), but this association is still quite high for adenocarcinomas (odds ratio, 19 to 21 for smokers > 30 cigarettes/day) [8].

In Korea, the lung cancer mortality in both sexes as well as the incidence in men have decreased, whereas the incidence in women has increased over the last few decades [9]. In addition, early detection by screening and the introduction of new chemotherapy and molecular targeted-agents may improve the survival of lung cancer patients. The objectives of the current study were to examine the trends in the lung cancer incidence, mortality, and survival in Korea. For the incidence and survival, the trends for each histological type were also assessed.

Materials and Methods

1. Lung cancer incidence

The Korea Central Cancer Registry (KCCR), a nation-wide, hospital-based cancer registry, was initiated by the Ministry of Health and Welfare, Korea in 1980. Since 1999, the KCCR expanded the cancer registration to cover the entire Korean population under the Population-Based Regional Cancer Registry program. The age- (5-year intervals) and sex-specific incidence rates and the number of cases for lung cancer patients between 1999 and 2012 were obtained from the Korea National Cancer Incidence Database. The histological subtypes of lung cancer were classified as follows: carcinomas (International Classification of Diseases for Oncology third edition morphological codes 8010-8576), sarcoma (8800-8811, 8830, 8840-8921, 8990-8991, 9040, 9044, 9120-9133, 9150, and 9540-9581), other specified cancers, including pulmonary blastoma, and unspecified (8000-8005). Carcinomas were further classified as follows: squamous cell carcinoma (8050-8078 and 8083-8084), adenocarcinoma (8140, 8211, 8230-8231, 8250-8260, 8323, 8480-8490, 8550-8551, 8570-8574, and 8576), small-cell carcinoma (8041-8045 and 8246), large-cell carcinoma (8010-8012, 8014-8031, 8035, and 8310), and other specified carcinomas.

The age-standardized rates (ASRs) were calculated using the mid-year population of 2000 as the standard population. The annual percent changes (APC) for the incidence rates were calculated based on a linear model using the following formula: $(\exp(b)-1) \times 100$, where b is the slope of the regression of the natural logarithm of the ASR in a calendar year [10]. The 95% confidence intervals were obtained with a standard error from the fit of the regression and the t-distribution function [11]. All analyses were stratified according to sex.

2. Lung cancer mortality

The lung cancer mortality data were obtained from the Statistics Korea for the years 1983-2013 (http://kosis.kr/). The ASRs for mortality, as well as the truncated rates for the four age groups (0-39, 40-59, 60-69, and ≥ 70 years) were estimated using the mid-year population of 2000 as the standard population. The trends in lung cancer mortality were tested using Joinpoint regression models, using Joinpoint software ver. 3.5.3 [12]. A maximum of four Joinpoints were allowed, and the default settings were used.

To evaluate the birth cohort effects on lung cancer mortality, 5-year age groups starting at age 20 years were categorized. The age-specific mortality rates were illustrated by the birth cohort. To evaluate the birth-cohort effects after adjusting for age and period effects, a log-linear model using the intrinsic estimator method was performed on the assumption that the number of deaths in each age group followed a Poisson distribution [13].

3. Lung cancer survival

The survival duration for registered lung cancer patients was determined as the interval between the date of the initial diagnosis and the date of death, date of loss to follow-up, or closing date for follow-up. The 5-year relative survival rates were calculated using the Ederer II method [14] based on an algorithm written in SAS by Dickman [15] with minor modifications. The 5-year relative survival rates of 1993-1997 and 2008-2012 were compared by the percentage changes. In addition, the excess risk model with a Poisson error structure was used to determine the difference in survival between 1993-1997 and 2008-2012 [16]. Statistical analysis was performed using Stata/SE 12.0 for Windows (StataCorp LP, College Station, TX) and SAS ver. 9.3 software (SAS Institute Inc., Cary, NC).

Results

1. Lung cancer incidence

In men, despite the increase in the crude incidence rates for lung cancer from 41.1/100,000 in 1999 to 60.9/100,000 in 2012 with an APC of 3.4%, the age-standardized incidence rate decreased from 51.8/100,000 in 1999 to 44.9/100,000 in 2012 with an APC of −0.9% (Table 1). The most frequent histological type was squamous cell carcinoma until 2010; however, since 2011, adenocarcinoma has been the most commonly diagnosed cancer. The number of new lung cancer

Table 1. CR and ASR per 100,000[a] for lung cancer and APC by sex and histological subtypes, the Korea Central Cancer Registry, 1999-2012

Histological group	Rate	Year														APC	95% CI	p-value
		1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012			
Men																		
Overall	Cases	9,722	9,788	10,473	10,956	11,187	11,961	12,497	12,682	13,182	13,593	14,240	14,914	15,319	15,350			
	CR	41.1	41.0	43.6	45.4	46.2	49.2	51.2	51.7	53.5	54.9	57.2	59.7	61.1	60.9	3.4	3.1 to 3.6	< 0.01
	ASR[a]	51.8	50.3	51.5	51.6	50.4	51.3	51.6	49.9	49.4	48.3	48.2	48.1	47.2	44.9	−0.9	−1.2 to −0.6	< 0.01
Carcinoma	Cases	6,967	6,947	7,916	8,262	8,735	9,373	9,861	10,361	10,907	11,354	12,148	12,741	13,173	13,365			
	CR	29.4	29.1	32.9	34.2	36.0	38.5	40.4	42.3	44.3	45.9	48.8	51.0	52.5	53.1	5.0	4.6 to 5.4	< 0.01
	ASR[a]	36.0	34.6	37.8	37.8	38.3	39.2	39.6	39.9	40.0	39.6	40.5	40.6	40.2	38.8	0.9	0.5 to 1.3	< 0.01
Squamous cell carcinoma	Cases	3,394	3,256	3,572	3,746	3,724	4,000	4,034	4,172	4,312	4,097	4,575	4,627	4,707	4,737			
	CR	14.3	13.6	14.9	15.5	15.4	16.4	16.5	17.0	17.5	16.5	18.4	18.5	18.8	18.8	2.4	2.0 to 2.9	< 0.01
	ASR[a]	17.7	16.3	17.2	17.3	16.4	16.9	16.4	16.2	16.0	14.3	15.4	14.8	14.3	13.7	−1.7	−2.2 to −1.2	< 0.01
Adenocarcinoma	Cases	1,731	1,838	2,205	2,177	2,404	2,561	2,859	3,041	3,232	3,780	4,024	4,414	4,900	5,045			
	CR	7.3	7.7	9.2	9.0	9.9	10.5	11.7	12.4	13.1	15.3	16.2	17.7	19.5	20.0	8.3	7.8 to 8.8	< 0.01
	ASR[a]	8.8	9.0	10.4	9.8	10.3	10.5	11.3	11.5	11.7	13.1	13.3	14.0	14.9	14.7	4.1	3.6 to 4.6	< 0.01
Small cell carcinoma	Cases	1,260	1,238	1,355	1,408	1,460	1,530	1,474	1,557	1,721	1,733	1,839	1,969	1,971	2,045			
	CR	5.3	5.2	5.6	5.8	6.0	6.3	6.0	6.4	7.0	7.0	7.4	7.9	7.9	8.1	3.5	3.1 to 4.0	< 0.01
	ASR[a]	6.4	6.1	6.4	6.5	6.4	6.4	5.9	6.0	6.3	6.1	6.1	6.2	6.0	5.9	−0.5	−0.9 to −0.1	0.01
Large cell carcinoma[b]	Cases	483	490	643	572	325	267	312	340	269	275	264	281	263	233			
	CR	2.0	2.1	2.7	2.4	1.3	1.1	1.3	1.4	1.1	1.1	1.1	1.1	1.0	0.9	−6.8	−9.3 to −4.2	< 0.01
	ASR[a]	2.5	2.4	3.1	2.6	1.4	1.1	1.3	1.3	1.0	1.0	0.9	0.9	0.8	0.7	−10.4	−12.8 to −7.9	< 0.01
Other specified carcinomas	Cases	99	125	141	359	822	1,015	1,182	1,251	1,373	1,469	1,446	1,450	1,332	1,305			
	CR	0.4	0.5	0.6	1.5	3.4	4.2	4.8	5.1	5.6	5.9	5.8	5.8	5.3	5.2	22.4	13.0 to 32.7	< 0.01
	ASR[a]	0.5	0.6	0.7	1.6	3.6	4.2	4.7	4.8	5.0	5.1	4.8	4.6	4.1	3.8	17.9	8.7 to 28.0	< 0.01
Sarcoma	Cases	17	16	28	14	25	16	21	27	30	24	38	21	28	30			
	CR	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1	4.0	0.5 to 7.7	0.03
	ASR[a]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.3	−2.3 to 5.0	0.46
Other specified cancer (including pulmonary blastoma)	Cases	9	10	8	9	10	10	10	16	11	11	9	6	11	10			
	CR	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	−0.2	−3.4 to 3.0	0.88
	ASR[a]	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	−3.9	−7.1 to −0.7	0.02
Unspecified cancer	Cases	2,729	2,815	2,521	2,671	2,417	2,562	2,605	2,278	2,234	2,204	2,045	2,146	2,107	1,945			
	CR	11.5	11.8	10.5	11.1	10.0	10.5	10.7	9.3	9.1	8.9	8.2	8.6	8.4	7.7	−3.0	−3.6 to −2.4	< 0.01
	ASR[a]	15.7	15.6	13.5	13.7	12.0	12.0	11.8	9.8	9.2	8.6	7.5	7.4	6.9	6.0	−7.2	−7.8 to −6.5	< 0.01

Table 1. Continued

Histological group	Rate		1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	APC	95% CI	p-value
Women																			
Overall	Cases		3,458	3,588	3,654	3,913	3,987	4,379	4,728	5,035	5,234	5,523	5,791	6,223	6,657	6,738			
	CR		14.7	15.2	15.3	16.3	16.6	18.1	19.5	20.7	21.4	22.4	23.4	25	26.6	26.8	5.2	4.8 to 5.5	< 0.01
	ASR[a]		12.9	12.9	12.7	13	12.8	13.5	14	14.5	14.4	14.5	14.6	15.2	15.6	15.3	1.7	1.4 to 2.0	< 0.01
Carcinoma	Cases		2,005	2,070	2,282	2,489	2,654	2,943	3,223	3,674	3,937	4,266	4,505	4,851	5,292	5,524			
	CR		8.5	8.7	9.6	10.4	11.0	12.2	13.3	15.1	16.1	17.3	18.2	19.5	21.1	22.0	8.1	7.7 to 8.6	< 0.01
	ASR[a]		7.8	7.8	8.3	8.7	8.9	9.6	10.1	11.1	11.4	11.9	12.1	12.6	13.2	13.2	4.7	4.3 to 5.1	< 0.01
Squamous cell carcinoma	Cases		364	357	367	386	375	427	427	503	443	439	440	485	523	473			
	CR		1.5	1.5	1.5	1.6	1.6	1.8	1.8	2.1	1.8	1.8	1.8	1.9	2.1	1.9	2.2	1.3 to 3.1	< 0.01
	ASR[a]		1.4	1.3	1.3	1.3	1.2	1.3	1.3	1.4	1.2	1.1	1.1	1.1	1.2	1.0	-1.7	-2.6 to -0.8	< 0.01
Adenocarcinoma	Cases		1,195	1,267	1,394	1,479	1,626	1,834	2,029	2,314	2,601	2,864	3,178	3,422	3,839	4,161			
	CR		5.1	5.4	5.8	6.2	6.8	7.6	8.4	9.5	10.6	11.6	12.8	13.7	15.3	16.5	10.0	9.6 to 10.5	< 0.01
	ASR[a]		4.7	4.8	5.2	5.2	5.5	6.1	6.5	7.2	7.7	8.2	8.7	9.1	9.8	10.2	6.6	6.2 to 7.1	< 0.01
Small cell carcinoma	Cases		266	240	276	294	321	273	287	327	319	366	308	392	384	409			
	CR		1.1	1.0	1.2	1.2	1.3	1.1	1.2	1.3	1.3	1.5	1.2	1.6	1.5	1.6	2.9	1.8 to 4.1	< 0.01
	ASR[a]		1.0	0.9	1.0	1.0	1.0	0.8	0.9	0.9	0.9	0.9	0.8	0.9	0.9	0.9	-1.1	-2.1 to 0.0	0.06
Large cell carcinoma[b]	Cases		132	148	179	184	88	77	86	95	82	71	78	88	81	77			
	CR		0.6	0.6	0.8	0.8	0.4	0.3	0.4	0.4	0.3	0.3	0.3	0.4	0.3	0.3	-6.2	-9.2 to -3.1	< 0.01
	ASR[a]		0.5	0.5	0.6	0.6	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	-9.9	-12.6 to -7.0	< 0.01
Other specified carcinomas	Cases		48	58	66	146	244	332	394	435	492	526	501	464	465	404			
	CR		0.2	0.2	0.3	0.6	1.0	1.4	1.6	1.8	2.0	2.1	2.0	1.9	1.9	1.6	19.1	11.3 to 27.5	< 0.01
	ASR[a]		0.2	0.2	0.3	0.5	0.8	1.1	1.3	1.3	1.4	1.4	1.4	1.2	1.2	1.0	14.9	7.4 to 22.9	< 0.01
Sarcoma	Cases		9	4	7	8	12	12	18	16	15	7	5	24	16	10			
	CR		0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.1	0.1	0.0	4.5	-2.6 to 12.1	0.20
	ASR[a]		0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.1	0.0	0.0	1.8	-4.8 to 8.8	0.58
Other specified cancer (include pulmonary blastoma)	Cases		4	4	5	5	2	2	1	11	1	7	3	7	10	5			
	CR		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.7	-7.2 to 15.9	0.48
	ASR[a]		0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.4	-8.1 to 11.9	0.76
Unspecified cancer	Cases		1,440	1,510	1,360	1,411	1,319	1,422	1,486	1,334	1,281	1,243	1,278	1,341	1,339	1,199			
	CR		6.1	6.4	5.7	5.9	5.5	5.9	6.1	5.5	5.2	5.0	5.2	5.4	5.3	4.8	-1.6	-2.3 to -1.0	< 0.01
	ASR[a]		5.1	5.1	4.3	4.3	3.8	3.8	3.8	3.3	2.9	2.6	2.5	2.5	2.4	2.0	-6.8	-7.5 to -6.1	< 0.01

CRs and ASRs were expressed per 100,000 people. CR, crude rate; ASR, age-standardized rate; APC, annual percent change; CI, confidence interval. [a]The Korean population in 2000 was used as standard population. [b]Large cell carcinoma includes giant cell, clear cell, and large cell undifferentiated carcinoma.
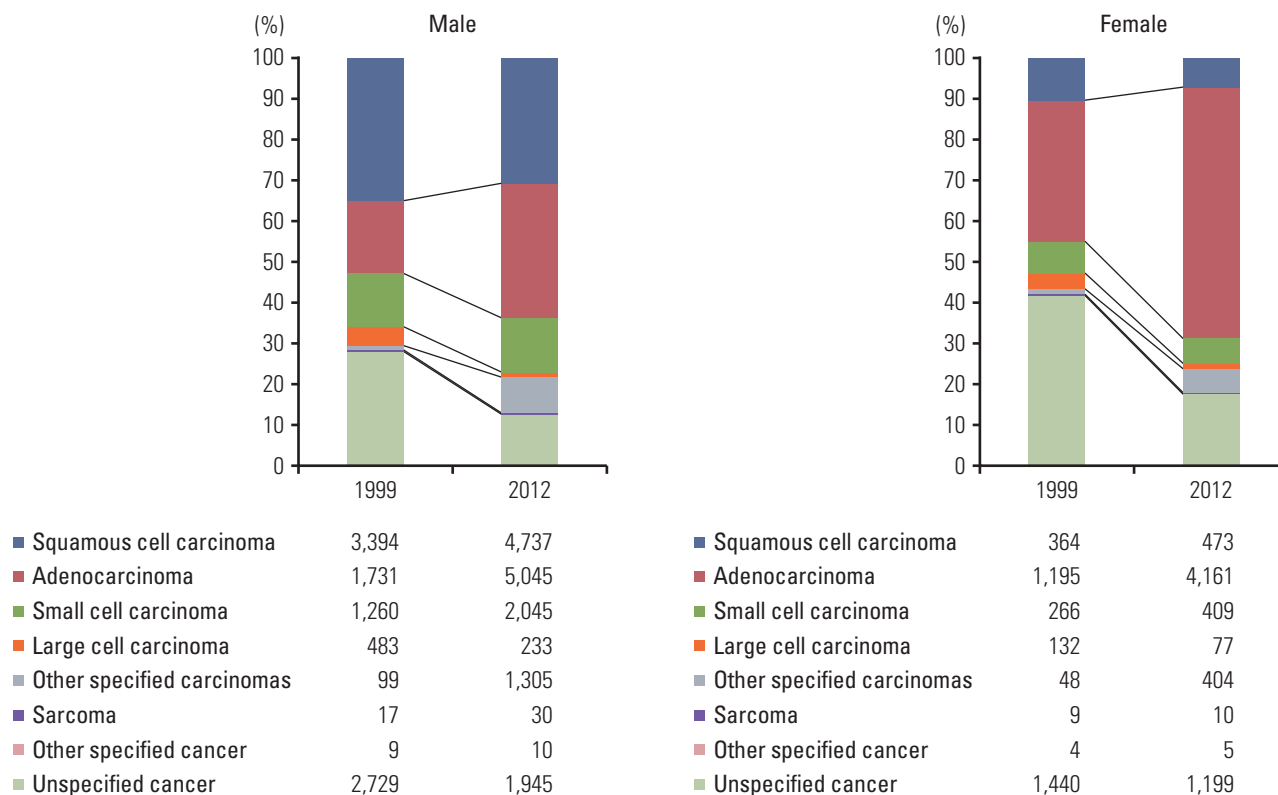
Fig. 1. Proportion of lung cancer cases according to the histologic types, based on the Korea Central Cancer Registry, 1999 and 2012.

cases increased from 9,722 in 1999 to 15,350 in 2012 (Table 1). The proportion of adenocarcinomas also increased during the same period (17.8% in 1999 and 32.9% in 2012), whereas the proportion of squamous cell carcinomas decreased (34.9% in 1999 and 30.8% in 2012) (Fig. 1). A significant decrease in ASRs for the incidence was observed for squamous cell carcinomas, small cell carcinomas, and large cell carcinomas, whereas the ASR for the adenocarcinoma incidence increased significantly (APC, 4.1%) between 1999 and 2012 (Table 1, Fig. 2A).

In women, both the crude rates and ASRs for the lung cancer incidence increased between 1999 and 2012 with an APC of 5.2% and 1.7% for the crude rate and incidence, respectively (Table 1). Adenocarcinoma was the most frequent histological subtype during this period. The proportion of adenocarcinomas increased from 34.5% in 1999 to 61.7% in 2012 (Fig. 1). Similar to men, both the crude rate and the ASR for adenocarcinoma incidence increased between 1999 and 2012, with an APC of 10% for the crude rate and 6.6% for ASR, whereas the ASRs for the incidence of squamous cell carcinomas, small cell carcinomas, and large cell carcinomas decreased (Table 1, Fig. 2B).

2. Lung cancer mortality

In both men and women, the number of deaths from lung cancer increased between 1983 and 2013 (S1 Table). In 2013, a total of 12,512 men and 4,653 women died from lung cancer, which places lung cancer as the most common cancer site for death in both sexes [9]. The lung cancer mortality rapidly increased between 1983 and 1994, with an APC of 9.4% for men and 7.6% for women (Table 2). From 1994, the slope of the increase began to stabilize, and since 2002, it started to decrease (Table 2). In stratified analysis according to age groups, there was a decline in mortality for the younger age groups in both men and women. For men, there was a significant decline in mortality from 1992 for the 40-59-year age group, from 2001 for the 60-69-year age group, and from 2002 for the ≥ 70 year age group. Similarly, for women, there was a decline in mortality from 1983 for the 0-39-year age group, from 1993 for the 40-59-year age group, from 1994 for the 60-69-year age group, and from 2002 for the ≥ 70 year age group.

Among elderly individuals aged ≥ 65 years, the ASR for the lung cancer mortality was highest among those born in the 1920s. When adjusting for age and period effects, the risk

A
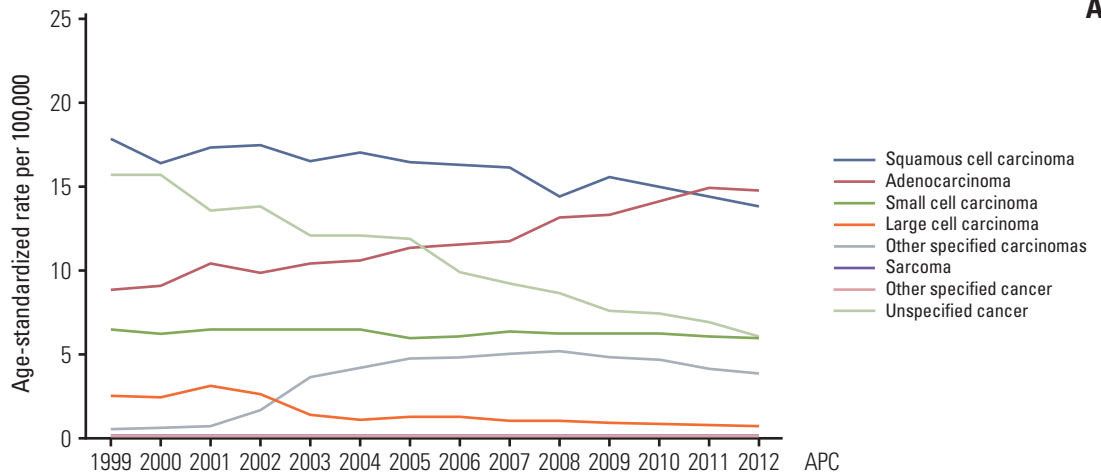
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	APC
Squamous cell carcinoma	17.7	16.3	17.2	17.3	16.4	16.9	16.4	16.2	16.0	14.3	15.4	14.8	14.3	13.7	−1.7
Adenocarcinoma	8.8	9.0	10.4	9.8	10.3	10.5	11.3	11.5	11.7	13.1	13.3	14.0	14.9	14.7	4.1
Small cell carcinoma	6.4	6.1	6.4	6.5	6.4	6.4	5.9	6.0	6.3	6.1	6.1	6.2	6.0	5.9	−0.5
Large cell carcinoma	2.5	2.4	3.1	2.6	1.4	1.1	1.3	1.3	1.0	1.0	0.9	0.9	0.8	0.7	−10.4
Other specified carcinomas	0.5	0.6	0.7	1.6	3.6	4.2	4.7	4.8	5.0	5.1	4.8	4.6	4.1	3.8	17.9
Sarcoma	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	1.3
Other specified cancer	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	−3.9
Unspecified cancer	15.7	15.6	13.5	13.7	12.0	12.0	11.8	9.8	9.2	8.6	7.5	7.4	6.9	6.0	−7.2

B
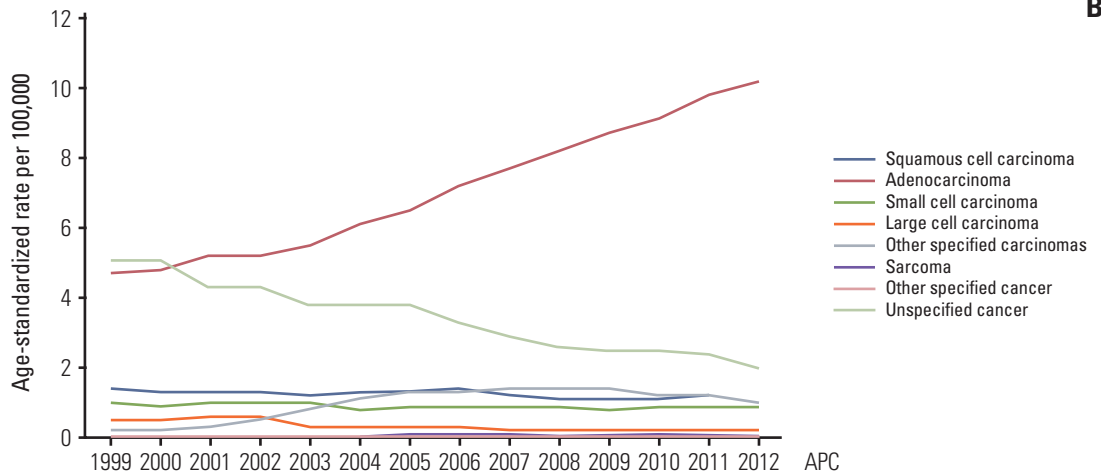
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	APC
Squamous cell carcinoma	1.4	1.3	1.3	1.3	1.2	1.3	1.3	1.4	1.2	1.1	1.1	1.1	1.2	1.0	−1.7
Adenocarcinoma	4.7	4.8	5.2	5.2	5.5	6.1	6.5	7.2	7.7	8.2	8.7	9.1	9.8	10.2	6.6
Small cell carcinoma	1.0	0.9	1.0	1.0	1.0	0.8	0.9	0.9	0.9	0.9	0.8	0.9	0.9	0.9	−1.1
Large cell carcinoma	0.5	0.5	0.6	0.6	0.3	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.2	−9.9
Other specified carcinomas	0.2	0.2	0.3	0.5	0.8	1.1	1.3	1.3	1.4	1.4	1.4	1.2	1.2	1.0	14.9
Sarcoma	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.0	0.0	0.1	0.0	0.0	1.8
Other specified cancer	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.4
Unspecified cancer	5.1	5.1	4.3	4.3	3.8	3.8	3.8	3.3	2.9	2.6	2.5	2.5	2.4	2.0	−6.8

Fig. 2. Age-standardized incidence rates of lung cancer according to the histologic types in men (A) and women (B), based on the Korea Central Cancer Registry, 1999-2012.

Table 2. Joinpoint analysis for lung cancer mortality at all ages and at age 0-39, 40-59, 60-69, and ≥70, in the Republic of Korea, 1983-2013

	Trend 1		Trend 2		Trend 3		Trend 4	
	Year	APC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)	Year	APC (95% CI)
Men								
All ages	1983-1994	9.4 (8.7 to 10.1)	1994-2002	1.6 (0.8 to 2.4)	2002-2013	−2.3 (−2.6 to −2.0)	-	-
0-39	1983-1993	−1.4 (−3.6 to 0.9)	1993-2013	−5.4 (−6.4 to −4.5)	-	-	-	-
40-59	1983-1992	6.1 (5.2 to 7.0)	1992-2000	−2.3 (−3.2 to −1.3)	2000-2013	−4.7 (−5.0 to −4.3)	-	-
60-69	1983-1987	13.7 (9.8 to 17.7)	1987-1994	9.4 (8.0 to 10.8)	1994-2001	−0.7 (−1.6 to 0.3)	2001-2013	−3.8 (−4.0 to −3.5)
≥70	1983-1994	14.2 (12.6 to 15.8)	1994-2002	6.3 (4.9 to 7.7)	2002-2013	−1.0 (−1.4 to −0.5)	-	-
Women								
All ages	1983-1994	7.6 (6.6 to 8.6)	1994-2002	1.6 (0.4 to 2.7)	2002-2013	−1.4 (−1.9 to −0.9)	-	-
0-39	1983-2013	−3.7 (−4.3 to −3.2)	-	-	-	-	-	-
40-59	1983-1993	4.7 (3.3 to 6.1)	1993-2013	−1.5 (−1.9 to −1.2)	-	-	-	-
60-69	1983-1994	8.7 (7.5 to 9.9)	1994-2013	−1.6 (−1.9 to −1.2)	-	-	-	-
≥70	1983-1994	13.6 (12.2 to 15.0)	1994-2002	5.4 (4.1 to 6.7)	2002-2013	−1.1 (−1.6 to −0.7)	-	-

Joinpoint regression models were used to detect significant changes in trends. APC, annual percent change; CI, confidence interval.

ratio for the lung cancer mortality was highest among those born between 1924 and 1929. After that, the younger generation had a lower risk of lung cancer mortality (Fig. 3A and B).

3. Lung cancer survival

Overall, the 5-year relative survival of lung cancer has improved significantly from 11.2% among patients diagnosed between 1993 and 1997 to 19.3% among patients diagnosed between 2008 and 2012 for men, and from 14.7% to 28.2%, respectively, in women (Table 3). An improved survival rate was observed for almost all histology groups, except for other specified carcinomas or other specified cancers. According to the histological types, adenocarcinomas showed the highest improvement for survival between 1993-1997 and 2008-2012, and an 8.6% improvement in the 5-year survival rate was observed for squamous cell carcinoma between 1993-1997 and 2008-2012. Otherwise, there has been little change in the 5-year survival rate of large cell carcinoma and sarcoma. Adenocarcinomas showed the highest 5-year survival rate in both men and women (27.1% for men and 38.3% in women) among patients diagnosed between 2008 and 2012.

Discussion

Despite the increase in the number of lung cancer patients, the ASR for the lung cancer incidence decreased between 1999 and 2012 in men in Korea, whereas it increased in women during this same time. Until 2010, squamous cell carcinoma was the most frequently diagnosed histological type in men, then adenocarcinoma was the most frequent histologic type. In women, adenocarcinoma has been the most frequent histological type since 1999.

The cigarette smoking rate has declined from 72% in 1992 to 42% in 2013 in adult men [17,18], whereas the smoking rates in adult women did not show significant changes, remaining at approximately 5%-8% [17]. It has been suggested that the reduction in tobacco consumption since the 1960s has been followed by a decrease in squamous cell carcinoma incidence, but not adenocarcinoma incidence in French men [19]. Moreover, the increase in adenocarcinoma incidence may be due to the detection of asymptomatic cases or improved diagnostic techniques [19]. On the other hand, an increase in adenocarcinoma may also be explained by the changes in cigarette manufacturing, including the introduction of filtered, lower tar- and lower nicotine-containing cigarettes [20]. Furthermore, nicotine-addicted smokers tend to inhale low-yield filtered cigarettes deeper and more inten-
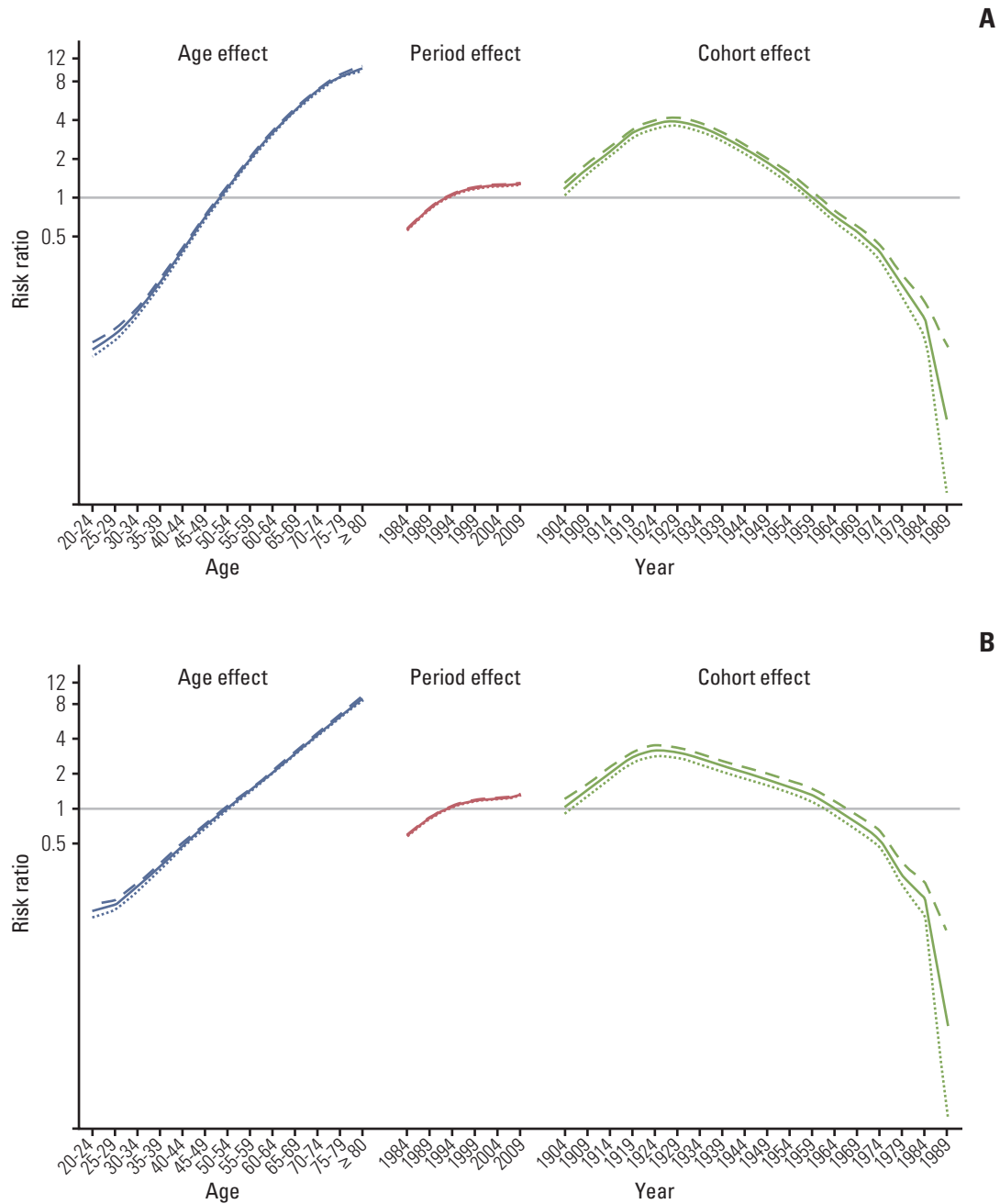
Fig. 3. Age-period-cohort analysis for lung cancer mortality in men (A) and women (B) in Korea.

sively than non-filtered higher-yield cigarettes to satisfy their nicotine needs; this leads to a more peripheral distribution of tobacco smoke in the lung and promotes peripheral tumors, such as adenocarcinomas [20,21].

A decrease in mortality in male lung cancer has been observed in many developed countries [4,22,23]. Lung cancer mortality is strongly influenced by tobacco consumption,

peaking 20-30 years after the peak in tobacco consumption [23,24]. Price and non-price tobacco control policies were introduced as early as 1986; these policies restricted advertising and included health warnings on cigarette packages in Korea [18]. In addition, in 1995, the Korean government passed the National Health Promotion Act and strengthened tobacco control policies [18]. The consequent decrease in lung

Table 3. Five-year relative survival rates of lung cancer patient by sex and histological subtypes, the Korea Central Cancer Registry, 1993-2012

Histological group	Year of diagnosis										Change[a] (%)	p-value[b]
	1993-1997		1998-2002		2003-2007		2008-2012		1993-2012			
	No.	5-Year survival (%)	No.	5-Year survival (%)	No.	5-Year survival (%)	No.	5-Year survival (%)	No.	5-Year survival (%)		
Overall total	**37,145**	**12.0**	**59,279**	**14.3**	**73,116**	**17.4**	**88,559**	**21.9**	**258,099**	**17.4**	**9.9**	**< 0.01**
Carcinoma	29,798	11.5	45,528	14.2	59,851	18.4	76,061	23.9	211,238	18.3	12.4	< 0.01
Squamous cell carcinoma	13,431	13.6	18,209	16.4	20,631	19.5	22,165	22.2	74,436	18.4	8.6	< 0.01
Adenocarcinoma	8,841	10.4	15,490	14.6	22,148	23.1	34,187	32.1	80,666	23.4	21.7	< 0.01
Small-cell carcinoma	5,179	6.2	7,467	8.0	8,739	7.5	10,432	8.0	31,817	7.6	1.8	< 0.01
Large-cell carcinoma	1,834	9.7	3,229	9.3	1,824	10.6	1,555	12.6	8,442	10.2	2.9	0.42
Other specified carcinomas	513	33.2	1,133	30.4	6,509	15.2	7,722	17.0	15,877	17.8	-16.2	< 0.01
Sarcoma	71	18.0	118	20.5	153	12.5	150	23.1	492	17.6	5.1	0.88
Other specified cancer	55	28.0	54	32.1	59	47.2	66	22.7	234	33.3	-5.3	0.35
Unspecified cancer	7,221	14.0	13,579	14.3	13,053	13.1	12,282	8.9	46,135	12.7	-5.1	< 0.01
Men												
Total	**28,695**	**11.2**	**44,342**	**12.9**	**53,690**	**15.9**	**62,863**	**19.3**	**189,590**	**15.5**	**8.1**	**< 0.01**
Carcinoma	23,575	11.1	35,235	13.5	45,080	17.0	54,900	21.0	158,790	16.6	9.9	< 0.01
Squamous cell carcinoma	12,099	13.7	16,493	16.5	18,705	20.0	20,099	22.7	67,396	18.7	9.0	< 0.01
Adenocarcinoma	5,366	9.0	9,263	12.4	12,747	19.9	19,087	27.1	46,463	19.8	18.1	< 0.01
Small-cell carcinoma	4,299	5.6	6,197	7.5	7,298	7.4	8,694	8.2	26,488	7.4	2.6	< 0.01
Large-cell carcinoma	1,450	9.4	2,500	8.9	1,424	10.5	1,198	13.4	6,572	10.1	4.0	0.17
Other specified carcinomas	361	28.6	782	25.0	4,906	14.0	5,822	15.9	11,871	16.1	-12.7	< 0.01
Sarcoma	45	16.8	82	15.6	95	7.0	110	21.5	332	14.3	4.7	0.89
Other specified cancer	44	28.2	36	25.2	44	37.4	42	18.2	166	28.1	-10.0	0.20
Unspecified cancer	5,031	11.2	8,989	10.3	8,471	10.0	7,811	7.2	30,302	9.7	-4.0	< 0.01
Women												
Total	**8,450**	**14.7**	**14,937**	**18.3**	**19,426**	**21.7**	**25,696**	**28.2**	**68,509**	**22.4**	**13.5**	**< 0.01**
Carcinoma	6,223	12.7	10,293	16.8	14,771	22.6	21,161	31.5	52,448	23.4	18.8	< 0.01
Squamous cell carcinoma	1,332	12.3	1,716	15.2	1,926	15.1	2,066	17.3	7,040	15.2	5.0	0.02
Adenocarcinoma	3,475	12.6	6,227	17.8	9,401	27.5	15,100	38.3	34,203	28.2	25.7	< 0.01
Small-cell carcinoma	880	9.1	1,270	10.5	1,441	8.3	1,738	7.1	5,329	8.7	-2.0	< 0.01
Large-cell carcinoma	384	10.8	729	10.8	400	10.7	357	9.5	1,870	10.7	-1.3	0.39
Other specified carcinomas	152	44.1	351	42.1	1,603	18.8	1,900	20.5	4,006	23.0	-23.6	< 0.01
Sarcoma	26	20.1	36	31.6	58	21.2	40	27.0	160	24.3	6.9	0.95
Other specified cancer	11	27.5	18	45.3	15	76.0	24	31.4	68	46.2	3.9	0.99
Unspecified cancer	2,190	20.5	4,590	22.0	4,582	18.9	4,471	11.8	15,833	18.5	-8.7	< 0.01

[a]Change (%) in the 5-year relative survival rates from 1993-1997 to 2008-2012, [b]p-values for changes in survival from 1993-1997 and 2008-2012 were derived by relative excess risk model.

cancer mortality since 2002 in Korea is consistent with previous reports [25].

The improvement in the lung cancer survival rate may be related to several factors, including the introduction of the target agents [26], earlier diagnosis [27], and a decrease in surgical mortality [27]. The introduction of (neo)adjuvant chemotherapy contributed to the improvement of stages I-III resectable non-small cell lung cancer patients [28]. Currently, adjuvant chemotherapy is applied to patients with resected stage II or III non-small cell lung cancer, and in patients with stage IB with a resected lesion of 4 cm or larger [29]. These findings appear to contribute to improved survival in adenocarcinoma. In addition, patients are now more likely to have access to health insurance and receive a timely diagnosis as well as high quality treatment and supportive care.

The limitations of the current study include a relatively high proportion of unspecified histology. The proportion of unspecified cancer was 31.6% in 1999, which improved to 14.2% in 2012. This can be explained in part by the improvements in diagnostic methods and in the quality of characterization, which may lead to more specific diagnoses. On the other hand, the substantial increase in adenocarcinoma cases cannot be explained by a misclassification of other histologic types to unspecified cancers. Another limitation regarding survival analysis was due to the limited information in stage information. Among the 88,655 lung cancer patients diagnosed between 2008 and 2012, the Surveillance, Epidemiology, and End Results stage information for 9,753 patients (11.0%) was missing [30]. The 5-year relative survival was 53.9% for localized cancer, 29.9% for regional cancer, 5.1% for distant cancer, and 15.8% for unknown stage cancers. Therefore, we cannot rule out the possibility that improved stage information might contribute to improvements in overall survival.

Despite these limitations, the KCCR provides reasonably high quality data (S2 Table). For instance, for lung cancer, the proportion of cases with a death certificate only was 10.8% in 1999 and improved to 3.3% in 2012. Moreover, the mortality/incidence ratio and the proportion of microscopic verification were in the acceptable ranges.

Conclusion

The lung cancer mortality began to decrease in both men and women in 2002. Since 1999, the of incidence lung cancer has decreased among men, whereas it has increased among women. Adenocarcinomas have become the most frequent histological type in both men and women. Finally, there has been an improvement in the 5-year relative survival of lung cancer patients.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (http://www.e-crt.org).

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

Acknowledgments

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