Analysis of the clinicopathological characteristics and their trends among patients with lung cancer undergoing surgery in a tertiary cancer hospital of north China during 2000–2013

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Background: Lung cancer is the primary cause of death among all cancers in China. However, clinical and pathological features and trends among patients with lung cancer in mainland China are largely unknown. This study analyzed the clinicopathological characteristics and trends of patients newly diagnosed as lung cancer and underwent surgery in a tertiary cancer hospital of north China between 2000 and 2013.

Methods: Data were collected retrospectively from medical records. Pathological diagnosis was confirmed by surgery or puncture, bronchoscopy, thoracoscopy, and sputum cytology.

Results: This study included 3,733 patients with lung cancer (2,252 male and 1,481 female; male-to-female 1.52:1). An increase in the incidence of lung cancer was observed among women. The most frequently observed pathology types were adenocarcinoma (ADC, 63.41%), squamous cell carcinoma (SQ, 24.48%), and small cell carcinoma (SCC, 3.08%). There was a decrease in the proportion of SQ cases and increase in ADC cases. The proportion of male patients with SQ and female patients with ADC increased. Differences between men and women in the distribution of lesions according to pathology were as follows: ADC and SQ were present in 49.73% and 35.92% of male patients, respectively, and in 84.20% and 7.09% of female patients, respectively. Comparing the time period 2000–2006 and 2007–2013, there were no changes in the distribution of pathology among men, while the proportion of ADC and SQ cases among women increased from 74.43% to 85.90% and decreased from 15.07% to 5.71%, respectively.

Conclusions: The proportion of female patients with lung cancer who could undergo surgery increased significantly. The proportion of patients with SQ decreased while that of ADC increased, and the increase of ADC was mainly due to the increase in the number of female patients with ADC.

Keywords: Lung cancer; China; clinicopathological characteristics; trend

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Introduction

Lung cancer is one of the most common malignant tumors, and its incidence has been increasing worldwide, including in China (1-4), posing a serious threat to public health. According to the 2013 data from the National Central Cancer Registry of China, lung cancer is the leading cause of cancer deaths among men and women, in cities as well as in rural areas (5). The World Health Organization (WHO) predicts that by 2035, there will be more than 1.25 million lung cancer deaths per year in China, which will become the country with the highest incidence of lung cancer (6).

As the incidence and mortality increase, studies have shown that the underlying pathology of lung cancer has also changed. Globally, the incidence of lung adenocarcinoma (ADC) has exceeded that of squamous cell carcinoma (SQ), the proportion of lung SQ cases in men has dropped significantly, and the proportion of lung ADC cases in women continues to rise (1,2,7-9). These findings are consistent with studies conducted in China (10-16). The epidemiological characteristics of lung cancer changes according to time, geographical location, and population subsets. This study examined the data of 3,733 patients with lung cancer undergoing surgery at the Peking University Cancer Hospital between 2000 and 2013, analyzing incidence trends, age of onset of cancer, and differences in the distribution according to sex and pathology of patients with lung cancer. The aim was to elucidate the clinicalepidemiological characteristics of lung cancer and the changes in its distribution according to histological types in China. This study provides a scientific basis for the prevention and treatment of lung cancer.

Methods

Study object

The data for this study were obtained from Peking University Cancer Hospital (Another name of this hospital is Beijing Cancer Hospital), which is an academic tertiary cancer hospital in northern China. The hospital is one of five institutes of National Key Discipline (oncology) in China and is also the Key laboratory of Carcinogenesis and Translational Research (Ministry of Education of China/ Beijing Municipality). Cancers treated include lung cancer, breast cancer, stomach cancer, colorectal cancer, esophageal cancer, liver cancer, thyroid cancer, cervical cancer, and other tumors frequently occurring in China. Over 80% of patients come from regions of north China, including Beijing, Hebei Province, Inner Mongolia Autonomous Region, Liaoning Province and Shanxi Province. Therefore, the characteristics of the patients admitted to Peking University Cancer Hospital are representative of those of patients in northern China. A total of 3,733 patients with lung cancer patients undergoing surgery were treated between January 2000 and December 2013, and in all patients a pathological diagnosis was made.

Data source

The data of patients with lung cancer treated between January 2000 and December 2013 were obtained from the Hospital Information Management System of Peking University Cancer Hospital. The inclusion criteria were (I) newly diagnosed and surgery performed at Peking University Cancer Hospital; (II) clear pathological diagnosis by surgery or puncture, bronchoscopy, thoracoscopy, sputum cytology. The exclusion criteria were as follows: (I) incomplete clinical or pathological data; (II) multiple hospitalizations and repeated information; (III) the primary tumor was not lung cancer and the participant had a secondary lung cancer; (IV) computed tomography (CT) scan of the chest suggested the possibility of lung cancer, but it was difficult to exclude other lung diseases, such as pneumonia, tuberculosis, and lung abscess. The cases of lung cancer in this study were categorized into 6 groups, according to the 2004 WHO histological classification of lung cancer (17), as follows: SQ, ADC, large cell carcinoma (LCC), adenosquamous carcinoma, small cell carcinoma (SCC) and others, which included carcinoid tumor, carcinomas of salivary gland type, and precancerous lesions.

The data collected comprised demographic characteristics and clinicopathological features of patients, including sex, age at diagnosis, pathological type, lesion location.

Statistical methods

EXCEL2007 software was used to construct a database and the data were filtered, sorted, and summarized. SPSS statistics software 19.0 (SPSS, Inc., an IBM Company, Chicago, IL, USA) was used for statistical description and statistical analysis, including the descriptive analysis of the data between 2000 and 2013, the comparative analysis of variables derived from the 2000–2006 data and the 2007– 2013 data. The count data analysis, trend analysis, and correlation analysis were performed using the chi-square test or chi-square test for trend, the Cox-Stuart trend test, and the Spearman correlation, respectively, and comparison between measurement data used *t*-test. A value of P<0.05 indicated that the difference was statistically significant.

Results

Number of patients admitted and gender distribution

Out of the total of 3,733 lung cancer patients newly diagnosed as lung cancer and undergoing surgery in the hospital, the trend test showed an increasing trend in the number of patients with lung cancer during the 14-year period (Z=-2.366, P=0.018). Of these, there were 2,252 males and 1,481 females, with a ratio of 1.52:1. The trend χ^2 test revealed that the sex distribution of patients newly diagnosed and treated between 2000 and 2013 changed (χ^2 =30.536, P<0.001), with an increasing proportion of female patients (*Table 1, Figures 1,2*).

Age distribution

The age of onset according to age groups was as follows: 60–74 years (45.69%) and 45–59 years (42.13%). Overall, the age distribution of patients admitted between 2007 and 2013 was significantly different to that of patients admitted between 2000 and 2006 (For total patients and male, female patients, the χ^2 values were 26.427, 15.845, and 9.231, respectively, and P values were <0.001, 0.001 and 0.026, respectively). Specifically, compared to the 2000– 2006 period, the proportion of patients aged 45–59 years admitted between 2007–2013 increased significantly while the proportion of patients aged 60–74 years decreased significantly, indicating a trend of patients suffering from 3975

lung cancer at younger age after seven years. Changes in age distribution according to time are presented in *Table 2*.

Pathological types of lung cancer

Time distribution of pathological types

Overall, the distribution according to pathological type of lung cancer was as follows: ADC 63.41%, SQ 24.48%,

 Table 1 Number of patients with lung cancer admitted per year to

 Peking University Cancer Hospital between 2000 and 2013 and the

 corresponding male-female patient ratios

Year	Male	Female	Male-female ratio	Total
2000	63	29	2.17	92
2001	38	21	1.81	59
2002	32	26	1.23	58
2003	44	14	3.14	58
2004	63	45	1.40	108
2005	97	33	2.94	130
2006	115	51	2.25	166
2007	177	87	2.03	264
2008	221	154	1.44	375
2009	235	130	1.81	365
2010	280	167	1.68	447
2011	278	212	1.31	490
2012	331	236	1.40	567
2013	278	276	1.01	554
Total	2,252	1,481	1.52	3,733

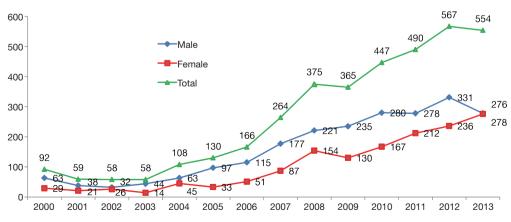


Figure1 Trends in the number of cases in 3,733 lung cancer patients undergoing surgery.

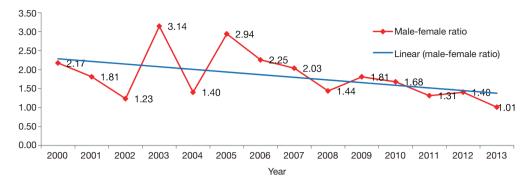


Figure 2 Trends in male-female patient ratio among admissions of patients with lung cancer undergoing surgery.

Table 2 Sex and age distribution of patients [n (%)]

		Ma	ale			Fen	nale		Total				
Age (years)	2000	2000–2006		2007–2013		2000–2006		2007–2013		2000–2006		2007–2013	
(years)	n	%	n	%	n	%	n	%	n	%	n	%	
≤44	48	10.62	116	6.44	29	13.24	104	8.24	79	11.77	220	7.18	
45–59	151	33.41	747	41.50	77	35.16	543	43.03	226	33.68	1,290	42.13	
60–74	229	50.66	839	46.61	106	48.40	560	44.37	335	49.93	1,399	45.69	
≥75	24	5.31	98	5.44	7	3.20	55	4.36	31	4.62	153	5.00	
Total	452	100.00	1,800	100.00	219	100.00	1,262	100.00	671	100.00	3,062	100.00	

and SCC 3.08%, with these types representing the most frequently diagnosed types of lung cancer. The proportion patients with ADC increased from 47.83% in 2000 to 74.73% in 2013, while that of patients with SQ decreased from 43.48% in 2000 to 17.69% in 2013. Correlation analysis showed that the proportions of ADC and SQ in each year were related to the years, while the proportions of SCC, LCC and adenosquamous carcinoma were not related to the years ($r_{s ADC}$ =0.873, P<0.001; $r_{s SQ}$ =-0.912, P<0.001; $r_{s sCC}$ =0.349, P=0.221; $r_{s LCC}$ =-0.278, P=0.335; $r_{s adenosquamous}$ carcinoma =-0.213, P=0.464). The results indicated that over the course study period, the proportion of patients with SQ showed an increasing trend (*Table 3* and *Figure 3*).

Distribution of the pathological types according to sex

Differences were observed in the sex distribution between the different pathological types of cancer (χ^2 =503.869, P<0.001). Among male patients, ADC (49.73%) and SQ (35.92%) were more frequently observed, while among female patients, the proportion of ADC and SQ was 84.20% and 7.09%, respectively. The proportion of ADC among female patients was considerably higher than that among male patients, while the proportions of SQ and SCC among male patients were considerably higher than those among female patients. The highest male-female ratio (7.70:1) was found among patients with SQ, while the proportions of male and female patients with ADC were comparable (0.90:1). SCC and LCC occurred more frequently among male patients, and the male-female ratios were 3.42:1 and 4.31:1, respectively. The trend χ^2 test showed that the distribution of patients with SCC and ADC according to sex changed from 2000 to 2013 (SQ χ^2 =7.752, P=0.005; ADC χ^2 =17.756, P<0.001), and an increasing trend in the proportion of male patients with SQ and of female patients with ADC was observed (*Tables 4*,5).

The distribution of pathological types of cancer among female patients changed during the overall course of this study (χ^2 =30.281, P<0.001). Specifically, the proportion of cases of ADC among female patients between 2007 and 2013 (85.90%) was higher than that reported between 2000 and 2006 (74.43%), while the proportion of cases of SQ

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Year	5	SQ	AI	ADC		CC		Adenosquamous carcinoma		SCC		Other types	
	n	%	n	%	n	%	n	%	n	%	n	%	-
2000	40	43.48	44	47.83	1	1.09	1	1.09	2	2.17	4	4.35	92
2001	19	32.20	33	55.93	1	1.69	2	3.39	2	3.39	2	3.39	59
2002	19	32.76	31	53.45	5	8.62	1	1.72	1	1.72	1	1.72	58
2003	18	31.03	32	55.17	3	5.17	2	3.45	0	0.00	3	5.17	58
2004	41	37.96	54	50.00	2	1.85	2	1.85	4	3.70	5	4.63	108
2005	39	30.00	75	57.69	2	1.54	0	0.00	3	2.31	11	8.46	130
2006	42	25.30	97	58.43	2	1.20	7	4.22	4	2.41	14	8.43	166
2007	78	29.55	145	54.92	4	1.52	9	3.41	11	4.17	17	6.44	264
2008	96	25.60	215	57.33	18	4.80	6	1.60	14	3.73	26	6.93	375
2009	91	24.93	226	61.92	16	4.38	5	1.37	14	3.84	13	3.56	365
2010	120	26.85	273	61.07	11	2.46	5	1.12	19	4.25	19	4.25	447
2011	85	17.35	347	70.82	12	2.45	8	1.63	17	3.47	21	4.29	490
2012	128	22.57	381	67.20	6	1.06	9	1.59	11	1.94	32	5.64	567
2013	98	17.69	414	74.73	2	0.36	9	1.62	13	2.35	18	3.25	554
Total	914	24.48	2,367	63.41	85	2.28	66	1.77	115	3.08	186	4.98	3,733

Table 3 Distribution of cases according to pathological type [n (%)]

SQ, squamous cell carcinoma; ADC, adenocarcinoma; LCC, large cell carcinoma; SCC, small cell carcinoma.

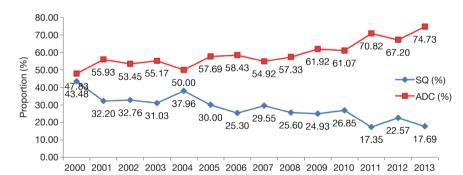


Figure 3 Trends in the proportions of SQ and ADC among patients. SQ, squamous cell carcinoma; ADC, adenocarcinoma.

decreased significantly (from 15.07% to 5.71%). Comparing the periods 2000–2006 and 2007–2013, the distribution of the pathological types of cancer among male patients did not change (χ^2 =8.852, P=0.115), although the proportion of SQ decreased while the proportion of ADC increased, as shown in *Table 6*.

Age distribution of the pathological types

Changes were observed in the age distribution of the

different pathological types of cancer (χ^2 =94.332, P<0.001), SQ and ADC most frequently occurred in the 60–74 years age group, while SCC occurred more frequently in the 45–59 years age group. Details of the pathological type of cancer according to age are presented in *Table* 7. Comparison between the 2000–2006 and 2007–2013 periods revealed that there were no changes in the average age of onset of ADC, SQ, and SCC among both male and female patients (*Table 8*).

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Dethological type	Male		Fei	male	Male-female ratio	Total		
Pathological type	n	%	n	%	Male-lemale ratio	n	%	
SQ	809	35.92	105	7.09	7.70	914	24.48	
ADC	1,120	49.73	1,247	84.20	0.90	2,367	63.41	
LCC	69	3.06	16	1.08	4.31	85	2.28	
Adenosquamous carcinoma	40	1.78	26	1.76	1.54	66	1.77	
SCC	89	3.95	26	1.76	3.42	115	3.08	
Other types	125	5.55	61	4.12	2.05	186	4.98	
Total	2,252	100.00	1,481	100.00	1.52	3,733	100.00	

Table 4 Distribution of the pathological types of lung cancer according to sex [n (%)]

SQ, squamous cell carcinoma; ADC, adenocarcinoma; LCC, large cell carcinoma; SCC, small cell carcinoma.

Table 5 Distribution of cases of SQ and ADC according to sex [n (%)]

Voor		SQ			ADC	
Year	Male	Female	Male-female ratio	Male	Female	Male-female ratio
2000	33	7	4.71	24	20	1.20
2001	17	2	8.50	17	16	1.06
2002	15	4	3.75	12	19	0.63
2003	15	3	5.00	23	9	2.56
2004	32	9	3.56	25	29	0.86
2005	36	3	12.00	46	29	1.59
2006	37	5	7.40	56	41	1.37
2007	69	9	7.67	77	68	1.13
2008	78	18	4.33	98	117	0.84
2009	84	7	12.00	117	109	1.07
2010	107	13	8.23	131	142	0.92
2011	78	7	11.14	162	185	0.88
2012	118	10	11.80	173	208	0.83
2013	90	8	11.25	159	255	0.62
Total	809	105	7.70	1,120	1,247	0.90

SQ, squamous cell carcinoma; ADC, adenocarcinoma.

Discussion

Lung cancer is a disease that severely threatens human health and social development. The GLOBOCAN2012 Cancer Report (3,18) released by the International Agency for Research on Cancer (IARC) shows that in 2012, approximately 1.8247 million new cases of lung cancer were predicted globally with 1.5899 million deaths. Lung cancer accounted for 12.95% of all new cases of malignant tumors and 19.38% of all deaths due to malignant tumors, and both were ranked highest. The number of new cases of lung cancer and the mortality rates among female lung cancer patients were significantly lower than those among men. In China, lung cancer has the highest incidence

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Table 6 Distribution of	nathological ty	mes of lung cancer	according to sex and	time [n	(%)	1
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		Ma	ale			Female				Total			
Pathological type	2000–2006		2007–2013		2000	2000–2006		2007–2013		2000–2006		-2013	
	n	%	n	%	n	%	n	%	n	%	n	%	
SQ	185	40.93	624	34.67	33	15.07	72	5.71	218	32.49	696	22.73	
ADC	203	44.91	917	50.94	163	74.43	1,084	85.90	315	46.94	2,001	65.35	
LCC	12	2.65	57	3.17	4	1.83	12	0.95	16	2.38	69	2.25	
Adenosquamous carcinoma	9	1.99	31	1.72	6	2.74	20	1.58	14	2.09	51	1.67	
SCC	14	3.10	75	4.17	2	0.91	24	1.90	16	2.38	99	3.23	
Other types	29	6.42	96	5.33	11	5.02	50	3.96	92	13.71	146	4.77	
Total	452	100.00	1,800	100.00	219	100.00	1262	100.00	671	100.00	3,062	100.00	

SQ, squamous cell carcinoma; ADC, adenocarcinoma; LCC, large cell carcinoma; SCC, small cell carcinoma.

Table 7 Distribution of pathological type of lung cancer according to age [n (%)]

Dethelesieeltype	≤	≤44		45–59		-74	2	75	Total	
Pathological type	n	%	n	%	n	%	n	%	n	%
SQ	48	5.25	372	40.70	448	49.02	46	5.03	914	100.00
ADC	181	7.64	962	40.59	1,108	46.75	119	5.02	2,370	100.00
LCC	6	7.06	31	36.47	43	50.59	5	5.88	85	100.00
Adenosquamous carcinoma	9	13.64	21	31.82	31	46.97	5	7.58	66	100.00
SCC	10	8.70	59	51.30	44	38.26	2	1.74	115	100.00
Other types	45	24.59	71	38.80	60	32.79	7	3.83	183	100.00
Total	299	8.01	1,516	40.61	1,734	46.45	184	4.93	3,733	100.00

SQ, squamous cell carcinoma; ADC, adenocarcinoma; LCC, large cell carcinoma; SCC, small cell carcinoma.

Table 8 Comparison of the age of onset of SQ, ADC, and SCC between male and female patients

Pathological type		Male p	atient		Female patient				
	2000–2006	2007–2013	t	Р	2000–2006	2007–2013	t	Р	
SQ	60.71	60.28	0.518	0.605	59.85	59.65	0.104	0.927	
ADC	61.05	61.23	1.043	0.970	59	59.06	-0.071	0.944	
SCC	56.02	58.77	-0.949	0.345	46.37	53.79	-1.317	0.200	

SQ, squamous cell carcinoma; ADC, adenocarcinoma; SCC, small cell carcinoma.

and mortality rate among all cancers, specifically, it has the highest incidence and mortality rate among men and the second highest incidence (after breast cancer) and the highest mortality rate among females (5). The survey showed that the incidence of lung cancer in Chinese cancer registration areas showed an increasing trend between 1989 and 2008 and that while the incidence increasing among both sexes, greater increases were observed among women. The male-female ratio among patients with lung cancer decreased from 2.47 in 1989 to 2.28 in 2008 (4). In this study, the clinical data of 3,733 newly diagnosed patients with lung cancer undergoing surgery between 2000 and 2013 in a representative tertiary cancer hospital of north China (Peking University Cancer Hospital) were analyzed in order to determine trends in lung cancer over the past 10 years and provide a scientific basis for the prevention and treatment of lung cancer in China.

The analysis showed that between 2000 and 2013 there was a rapid increase in the number of patients with lung cancer undergoing surgical treatment in this hospital, which reflected the rapid increase in the incidence of lung cancer reported among the Chinese population (4,5,10-12). Furthermore, there was also an association between the rapid rise of the influence of research hospitals in the field of cancer diagnosis and treatment in China. The malefemale ratio of all patients was 1.52:1, although this ratio decreased from 2.17:1 in 2000 to 1.01:1 in 2013, with an increase in the incidence of lung cancer among women. Regarding the age distribution of lung cancer, this was more frequently reported among in the middle-aged and elderly population, with the highest number of cases observed among subjects aged 60-74 years. However, compared to the period 2000–2006, the proportion of patients with lung cancer aged between 45-59 years considerably increased and the proportion of patients aged between 60-74 years significantly decreased between 2007 and 2013.

The primary pathological type of patients was ADC, followed by SQ and SCC. The proportion of patients admitted with ADC increased from 47.83% in 2000 to 74.73% in 2013, while that of patients admitted with SQ dropped from 43.48% in 2000 to 17.69% in 2013. Reports indicate that in the 1950s, the most frequent histological type of lung cancer was SQ, with ADC accounting for only approximately 5% of cases. However, the incidence of ADC has risen rapidly in recent years (7-12). Between 2000 and 2003, the number of patients with ADC accounted for 47% of all patients with lung cancer in the United States (19). Between 1998 and 2007, in urban areas of Beijing, the proportion of patients with ADC among all patients with lung cancer increased from 42.83% to 46.80% and ADC accounted for 60.83% of all lung cancer among women (14). The findings of this study are consistent with the above reports. It should be noted that the clinical condition of patients with lung cancer who are suitable for surgical treatment is generally better than that of patients with lung cancer in general and that there are differences

between these groups in terms of cancer pathology (20-22). Therefore, this study does not completely represent the situation of all patients with lung cancer. The increase in the proportion of cases of lung cancer patients with ADC in this study was first due to the increased incidence of ADC patients worldwide, including the Chinese population, and the number of ADC patients who could undergo surgery increased correspondingly. The increase in the incidence of lung cancer may also be attributed to the increased accuracy of pathological diagnosis, with the aid of immunohistochemical techniques. Many ADC cases that were previously difficult to identify can now be diagnosed, including poorly differentiated solid type ADC that were difficult to identify (23). Furthermore, ADC lesions are peripheral and are relatively simple to excise. Conversely, SQ lesions are generally more central and are technically more difficult to excise with an increased risk to the patient, and the physicians or patients having intentions for surgery are also relatively less.

Male and female patients exhibited different pathological types of cancer. Among female patients, ADC was dominant (84.20%) and the proportion of ADC increased from 74.43% between 2000 and 2006 to 85.90% between 2007 and 2013, while the proportion of cases of SQ decreased from 15.07% to 5.71%. Among male patients, ADC and SQ were more frequently observed, and the pathological types of lesion did not change significantly between the period 2000-2006 and 2007-2013. The highest malefemale ratio (7.70:1) was found among patients with SQ while the proportion of male and female patients with ADC was comparable (male-female ratio 0.90:1). Patients with SCC and LCC were more frequently male, and the corresponding male-female ratios were 3.42:1 and 4.31:1, respectively. There was no change in the average ages of onset of ADC, SQ, and SCC in both male and female patients between the period 2000-2006 and 2007-2013.

This study showed that the increase in the proportion of patients admitted for ADC was mainly due to the increase in the number of female patients, who were mostly diagnosed with ADC. In recent years, there has been an increased focus on the rising incidence of lung cancer among women. In some developed countries, the incidence of lung cancer in women has exceeded that of men, and ADC has been reported to be the main pathological type of lung cancer among women (2,7). Studies have shown that environmental pollution, cooking fumes, passive smoking, a family history of cancer, and increases in economic income, as well as social and psychological stress, are strongly associated with

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the development of ADC in women (2,3,5,6,24,25). These findings indicate that changes in social and environmental factors were an important reason for the increase in ADC among women, which deserved more attention.

In summary, the increase in the number of patients with lung cancer admitted for surgical treatment reflected the increasing incidence of lung cancer in China. The most frequent histological types of lung cancer were ADC, SQ, and SCC. However, over the years, the distribution of pathological types changed significantly. The proportion of patients admitted with SQ showed a downward trend while that of patients admitted with ADC showed an upward trend. In particular, the proportion of female patients with ADC increased. However, this single institute study may not fully represent the lung cancer status of the whole region in China.

But anyway, it is anticipated that the detection rates of early lung cancer will be higher with the implementation of routine medical examination and improvements in modern diagnostic and treatment technology for lung cancer, particularly, the use of low-dose spiral CT in screening programs (10,26,27). Therefore, increasing numbers of patients with lung cancer will be able to undergo surgery. It is important to promote health education, disseminate knowledge of prevention and treatment of lung cancer, and raise public awareness of regular physical examination, to improve the early diagnosis of lung cancer.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study had been examined and certified by Ethics Committee of Beijing Cancer Hospital (2017-031).

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