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Changes in the Demographics and Prognoses of Patients with Resected Non-Small Cell Lung Cancer: A 20-Year Experience at a Single Institution in Korea

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The demographics and prognosis of non-small cell lung cancer patients have changed during the last few decades. We conducted this study to assess the change in demographics and prognosis in resected non-small cell lung cancer patients during a 20-yr single-institution study in Korea. We retrospectively reviewed the medical records of 2,076 non-small cell lung cancer patients who underwent pulmonary resection between 1990 and 2009. Their clinical characteristics and survival were analyzed over a five-year period. With time, the proportions of female, adenocarcinoma, stage IA, and lobectomy patients increased, whereas the proportions of male, squamous cell carcinoma, stage IIIA, and pneumonectomy patients decreased. These demographic changes caused improved prognosis. The five-year survival rate of all patients was 53.9%. The five-year survival rate increased from 31.9% in 1990-1994, to 43.6% in 1995-1999, 51.3% in 2000-2004, and 69.7% in 2005-2009 ($P < 0.001$). In conclusion, among patients with resected non-small cell lung cancer, the proportions of female, adenocarcinoma, stage IA, and lobectomy patients have increased, and the five-year survival rate has gradually improved during the last 20 yr in Korea.

Key Words: Demography; Prognosis; Change; Carcinoma; Non-Small Cell Lung Cancer

INTRODUCTION

Lung cancer is the leading cause of cancer deaths in the Western world as well as in Korea (1-3). Non-small cell lung cancer (NSCLC) constitutes more than 80% of lung cancer cases, and surgery remains the only potentially curative treatment for early stage lung cancer. During the last few decades, the clinical profile of NSCLC patients who are candidates for surgical resection has changed dramatically. According to the Japanese Joint Committee for Lung Cancer Registration (JJCLCR), the proportions of patients who are female, have stage IA disease, and have adenocarcinoma have increased, and the five-year survival rate has gradually improved from 47.2% in 1989, to 52.6% in 1994, to 61.4% in 1999, and to 69.6% in 2004 (4-7). As such, it is important to understand the demographics, tumor-related background, and the prognosis by related factors and stage. In addition, determining trends in those parameters will be helpful in developing nation-specific strategies for lung cancer treatment. In this study, we analyzed 20 yr of single-institution data to identify the recent surgical outcomes and trends related to non-small cell lung cancer surgery in Korea.

MATERIALS AND METHODS

Patients

We reviewed the records of 2,076 patients with NSCLC who underwent pulmonary resection at our institute from January 1990 to December 2009. Pathological staging was based on the 2009 TNM classification system (8). Tumor histology was categorized according to the World Health Organization classification. Lymph node status was assessed according to the system defined by Mountain and Dresler (9). Lobectomy and systematic lymph node dissection were the procedures of choice, regardless of clinical stage. Patients with stage I-IIIA disease were indicated for surgical resection. All patients were followed either until death or the last follow-up date (December 1, 2011).

Statistical analysis

The duration of survival was defined as the interval between the date of surgery and either the date of death or the last follow-up date. Survival curves were estimated using the Kaplan-Meier method, and differences in survival were assessed by the log-rank test. In the analysis of pathologic stage and survival, the patients (n = 169) who received induction treatment were

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excluded. A P value less than 0.05 was considered significant. The data were analyzed using SPSS for Windows (Statistical Package for the Social Sciences, SPSS Inc. Chicago, IL, USA).

Ethics statement

The institutional review board of Yonsei University College of Medicine approved this retrospective study (4-2012-0505). Informed consent was waived by the board.

RESULTS

Patient characteristics

The 2,076 patients included 558 females and 1,518 males with a median age of 62 yr (range, 10 to 90 yr). The median follow-up

Table 1. Clinical and pathologic characteristics of 2,076 patients

Parameters	No. of patients (%)
Age (median, range)	62.0 (10-90)
Sex	
Male	1,518 (73.1)
Female	558 (26.9)
Type of resection	
Pneumonectomy	559 (26.9)
Bilobectomy	229 (11.0)
Lobectomy	1,234 (59.4)
Other	54 (2.6)
Histologic subtype	
Squamous cell carcinoma	902 (43.4)
Adenocarcinoma	923 (44.5)
Large cell	89 (4.3)
Other	162 (7.8)
Pathologic stage	
IA	358 (18.8)
IB	441 (23.1)
IIA	289 (15.2)
IIB	207 (10.9)
IIIA	503 (26.4)
IIIB	65 (3.4)
IV	44 (2.3)

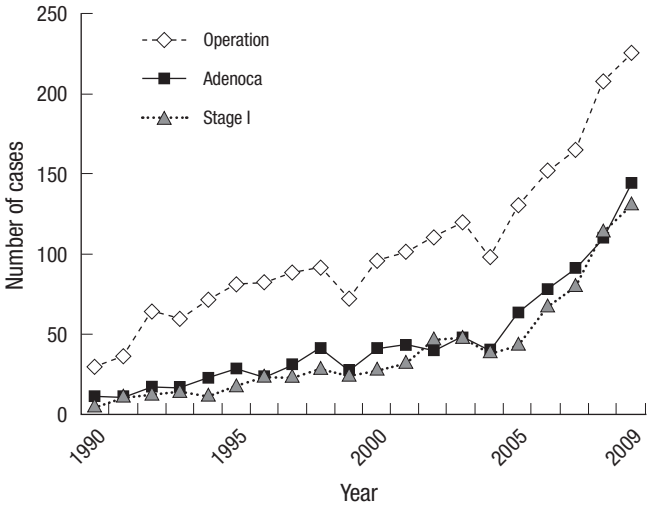

Fig. 1. Number of NSCLC patients with resection, adenocarcinoma and stage I according to time. The proportion of patients with pathologic stage I disease and adenocarcinoma increased from 16.6% (5/30) and 33.3% (10/30), respectively, in 1990 to 58.2% (131/225) and 64.0% (144/225), respectively, in 2009 (NSCLC: non-small cell lung cancer).

Table 2. Proportion of cases according to time period

Parameters	1990-1994	1995-1999	2000-2004	2005-2009
No. of patients	260	415	523	878
Age (yr, mean ± SD)	57.8 ± 9.0	59.7 ± 9.7	60.7 ± 10.1	62.5 ± 10.0
Sex				
Male	214 (82.3%)	328 (79.0%)	389 (74.4%)	587 (66.9%)
Female	46 (17.7%)	87 (21.0%)	134 (25.6%)	291 (33.1%)
Histology				
Squamous	151 (58.1%)	210 (50.6%)	233 (44.6%)	308 (35.1%)
Adenocarcinoma	77 (29.6%)	151 (36.4%)	211 (40.4%)	484 (55.1%)
Other	32 (12.3%)	54 (13.0%)	79 (15.0%)	86 (9.8%)
Procedure				
Pneumonectomy	152 (58.5%)	205 (49.4%)	133 (25.4%)	69 (7.9%)
Bilobectomy	21 (8.1%)	66 (15.9%)	61 (11.7%)	81 (9.2%)
Lobectomy	78 (30.0%)	136 (32.7%)	314 (60.0%)	706 (80.5%)
Other	9 (3.5%)	13 (3.1%)	15 (2.9%)	22 (2.5%)
pStage				
IA	14 (6.0%)	41 (10.6%)	68 (14.6%)	235 (28.7%)
IB	40 (17.0%)	76 (19.6%)	123 (26.4%)	202 (24.7%)
IIA	44 (18.7%)	53 (13.7%)	74 (15.9%)	118 (14.4%)
IIB	27 (11.5%)	47 (12.1%)	52 (11.2%)	81 (9.9%)
IIIA	92 (39.1%)	136 (35.1%)	117 (25.1%)	158 (19.3%)
IIIB	14 (6.0%)	21 (5.4%)	17 (3.6%)	13 (1.6%)
IV	4 (1.7%)	14 (3.6%)	15 (3.2%)	11 (1.3%)
Tumor size (cm)	4.5 ± 2.5	4.2 ± 2.2	3.8 ± 2.2	3.4 ± 2.0
Smoking History				
Yes	150 (57.7%)	263 (63.4%)	294 (56.2%)	460 (52.4%)
No	110 (42.3%)	152 (36.6%)	229 (43.8%)	418 (47.6%)

time was 37.3 months (range, 0 to 261.9 months). All patient characteristics are summarized in Table 1. The overall five-year survival rate was 53.9%. The five-year survival rate was 85.6% for stage IA, 71.7% for IB, 48.4% for IIA, 46.2% for IIB, 33.1% for IIIA, 5.2% for stage IIIB, and 17.1% for stage IV.

Trends in characteristics

In the time period from 1990 to 2009, the proportion of patients with pathologic stage I disease increased from 16.6% (5/30) in 1990 to 58.2% (131/225) in 2009. In terms of lung cancer subtype, the proportion of adenocarcinomas increased annually from 33.3% (10/30) in 1990 to 64.0% (144/225) in 2009 (Fig. 1), while the proportion of squamous cell carcinomas decreased annually from 56.6% (17/30) in 1990 to 30.2% (68/225) in 2009. This shift in the distribution of tumor subtypes was prominent after the mid-2000s.

Patients were divided into the following four groups based on their year of surgery: 1990-1994, 1995-1999, 2000-2004, and 2005-2009. The mean age of the patients at the time of the operation increased over time. The proportions of female, adenocarcinoma, lobectomy, and pathologic stage Ia patients increased. The proportions of male, squamous histology, pneumonectomy and stage IIIa patients decreased over time (Table 2).

Trends in survival

The overall five-year survival rate of all patients was 53.9%. The overall survival rate improved over time, increasing from 31.9% in 1990-1994, to 43.6% in 1995-1999, to 51.3% in 2000-2004, and to 69.7% in 2005-2009 ($P < 0.001$, Fig. 2). This tendency was similar for every pathologic stage. The five-year survival rate increased from 85.7% in 1990-1995 to 89.2% in 2005-2009 for stage IA, from 57.5% to 83.6% for stage IB, from 25.0% to 55.3% for stage IIA, from 48.1% to 49.5% for stage IIB, from 16.3% to 53.9% for stage IIIA, from 7.1% to 11.5% for IIIB, and from 0% to 32.7% for stage IV (Table 3).

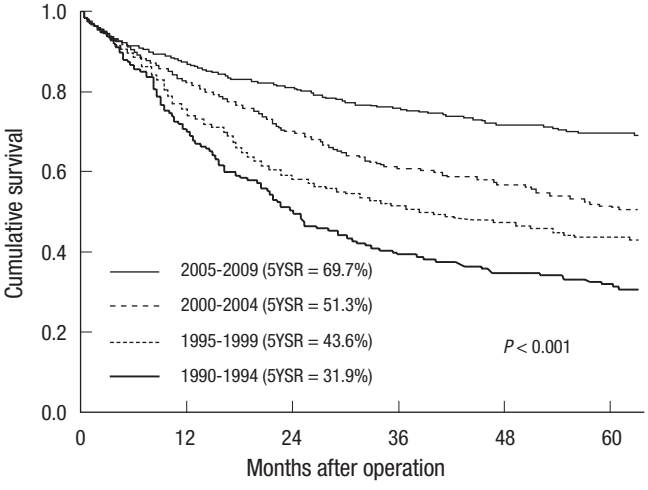

Fig. 2. Postoperative overall survival curves for patients according to time period. The five-year survival rate improved over the 20-yr study period and there were significant differences among the groups ($P < 0.001$) (5YSR: Five-year survival rate).

DISCUSSION

The demographics and prognoses of non-small cell lung cancer patients undergoing surgery at a single Korean institution have changed over the last 20 yr. The proportions of patients who are female, underwent lobectomy, have stage IA disease, and have adenocarcinoma have increased, and the five-year survival rate has gradually improved from 31.9% in 1990-1994 to 43.6% in 1995-1999, to 51.3% in 2000-2004, and to 69.7% in 2005-2009.

The lung cancer incidence in Western countries (North America, Western Europe, Australia) has stabilized over the past decades (10). However, there have been major shifts in the frequencies of the various histological types of lung cancer, with significant increases in the incidence of adenocarcinoma, and a corresponding decrease in the incidence of squamous cell cancer. For example, registry data from the USA indicated that the ratio of squamous carcinomas to adenocarcinomas was approximately 17:1, and by 1995 these two histological types of cancer were nearly equal in incidence. Although lung cancer data are not extensively available for Asian populations, the same pattern of change has been observed (11). In Taiwan, a study of over 10,000 cases over the period from 1970 to 1993 showed that the incidence of squamous carcinoma decreased from 46.4% to 36.2% in men, whereas adenocarcinoma increased from 30% to 36% in men and from 50.7% to 64.8% in women, such that adenocarcinoma has now become the most common cancer cell type (12). Similar patterns were found in Singapore, Korea, Hong Kong and Japan (13-16). This study also showed a similar pattern with surgically resected lung cancer cases and this shift in the distribution of cancer types was prominent after the mid-2000s (Fig. 1).

The prognosis of surgical resection of NSCLC was not promising. Despite "curative resection," more than 70% of patients with NSCLC in one study experienced recurrence (17). The five-

Table 3. Five-year survival according to time period

Pathological stage	1990-1994	1995-1999	2000-2004	2005-2009
Overall	31.9%	43.6%	51.3%	69.7%
Sub-stage				
IA	85.7%	78.0%	80.9%	89.2%
IB	57.5%	71.1%	65.0%	83.6%
IIA	25.0%	50.9%	52.7%	55.3%
IIB	48.1%	36.2%	48.1%	49.5%
IIIA	16.3%	28.7%	29.9%	53.9%
IIIB	7.0%	0%	5.9%	11.5%
IV	0%	0%	26.7%	32.7%
Stage				
I	64.8%	73.5%	70.7%	86.5%
II	33.8%	44.0%	50.8%	53.0%
III	15.1%	24.8%	26.9%	50.7%
IV	0%	0%	26.7%	32.7%

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Table 4. Trend in surgical results over time

Authors	Histology	Pathologic stage	Year of resection five-year survival rate					
Koike et al. (19)	NSCLC	0-IV	1963-1977 33.7%	1978-1986 51.8%	1987-1992 58.4%			
Fang et al. (20)	NSCLC	I-IV	1960s 44.6%	1970s 44.2%	1980s 38.1%	1990s 49.8%		
Yoshino et al. (21)	NSCLC	0-IV		1970s 30.3%	1980s 41.6%	1990s 50.1%		
JJCLC (3-6)	All	0-IV			1989 47.2%	1994 52.6%	1999 61.4%	2004 69.6%
This report	NSCLC	I-IV			1990-1994 31.9%	1995-1999 43.6%	2000-2004 51.3%	2005-2009 69.7%

NSCLC, non-small cell lung cancer; JJCLC, Japanese Joint Committee for Lung Cancer Registration.

year survival rate after resection was 42.6% according to Naruke et al. (18) and 41.4% according to van Rens et al. (19). However, it is not surprising that postoperative survival is changing with each decade based on the date of resection, histology, and the distribution of stages.

There have been a few reports focusing on the change in surgical results over time (Table 4). Koike et al. (20) divided the dates of resection into three periods and reported that the proportion of stage IA cases increased and that the five-year survival rate improved over time (33.7% in 1963-1977, 51.8% in 1978-1986, and 58.4% in 1987-1992). Fang and coworkers (21) compared the NSCLC surgical results from four periods: 1960s, 1970s, 1980s, and 1990s. They reported that the five-year survival rate improved with some influencing factors, such as the rate of postoperative complications, lymph node dissection, and combination therapy. Yoshino and coworkers (22) compared the surgical results for NSCLC resected in the three decades from 1975 to 1998 and reported that the five-year survival rates improved (30.3% in the 1970s, 41.6% in the 1980s, and 50.1% in the 1990s) due to an increasing number of female patients with adenocarcinoma, more frequent detection of early disease, and effective elimination of unresectable cases.

The Japanese Joint Committee for Lung Cancer Registration (JJCLCR) reported that the proportions of patients who are female, have stage IA disease, and have adenocarcinoma have increased, and the five-year survival rate has gradually improved, from 47.2% in 1989, to 52.6% in 1994, to 61.4% in 1999, and to 69.6% in 2004 (4-7). In this study, the postoperative five-year survival rate in Korea improved from 31.9% in 1990-1994, to 43.6% in 1995-1999, to 51.3% in 2000-2004, and to 69.7% in 2005-2009, mainly due to increased proportions of female patients, pathologic stage IA cases and decreased pneunonectomy cases. The prognosis for this surgical result is similar to that in the JJCLCR reports, and has changed more dramatically due to the prominent change in demographics after the mid-2000s. The recent favorable surgical outcomes including those presented by the JJCLCR and in this report suggest that good surgical results for NSCLC have been achieved.

With regard to the change in the five-year survival rate according to sub-staging groups, the data are not sufficient to fully evaluate the prognosis of all stages in each period due to the relatively small number of cases from our single institution. However, the trend of improvement in survival rate was noted in all subgroups. This improvement in each stage is likely due to a decreased mean tumor size (from 4.5 cm in 1990-1994 to 3.4 cm in 2005-2009), decreased proportion of pneumonectomy cases, standardization of adjuvant chemotherapy, increased proportion of female patients, and increased proportion of adenocarcinoma, which is a good target for recently developed chemotherapy.

To the best of our knowledge, this is the first report from Korea assessing the recent trends in demographics and prognoses for resected NSCLC cases. In conclusion, the clinical profiles of resected non-small cell lung cancer have changed in the last 20 years in Korea. The proportions of female, stage IA, lobectomy, and adenocarcinoma patients have increased, and the five-year survival rate has gradually improved from 31.9% in 1990-1994, to 43.6% in 1995-1999, to 51.3% in 2000-2004, and to 69.7% in 2005-2009.

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