

A Statistical Study of Lung Cancer in the Annual of Pathological Autopsy Cases in Japan, from 1958 to 1997, with Reference to Time Trends of Lung Cancer in the World

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Lung cancer cases (66 650 males and 20 890 females) registered in the Annual of Pathological Autopsy Cases in Japan, between 1958 and 1997, were analyzed with regard to sex, age and histology. They were subdivided into decades (periods I to IV), and compared with the Japanese mortality statistics, with which they were in good correspondence. Although the autopsy rate is decreasing, more than 10% of the total lung cancer deaths in Japan were registered by 1990. Among autopsied cases, the incidence of lung cancer cases increased from 6% to 12% in males and from 3% to 6% in females. From period III, lung cancer in males became the most frequent, and was the second most frequent cancer in females after gastric cancer. As for the histological distribution, adenocarcinoma was the most frequent and squamous cell carcinoma was the next most frequent in both sexes. Recently, a significant increase in adenocarcinoma and a significant decrease in squamous cell carcinoma have been observed in both sexes. The peak ages shifted from the 60s to the 70s and a significant rise in the mean ages were observed. The male-to-female ratios and the ratio curves by histological and age group were high for squamous cell carcinoma and small cell carcinoma, while they were low for the total and adenocarcinoma. With the recently acquired data on lung cancer in Asian countries, and from the male-to-female ratios and the status of smoking rates, lung cancer in the world at present was divided into three groups; North America, Europe and Asia. The possibility of one group changing to resemble another and of groups converging in the near future is suggested.

Key words: Lung cancer autopsy cases — Age and sex — Histological types — Male-to-female ratio — Cigarette smoking

In North America^{1,2)} and some European countries,^{3,4)} due to successful anti-smoking policies, the lung cancer rate is currently decreasing. In Japan, the lung cancer rate is still increasing,^{5,6)} and the transition of lung cancer cases to the older generation is continuing.^{5,6)} Japan also has a high percentage of adenocarcinoma in both sexes.^{7,8)}

Since 1958, the Japan Society of Pathology has published “the Annual of Pathological Autopsy Cases in Japan” (the Annual),⁹⁾ which contains a brief summary of almost all autopsy cases in major Japanese hospitals.

Although the autopsy rate is decreasing in Japan, the Annual⁹⁾ still keeps a nationwide record of almost all autopsies performed. The largest amounts of data covered 5.3% of all the deaths in 1985 and 14.0% of the total number of lung cancer deaths in 1980.⁵⁾ In the present study, all the lung cancer cases registered from 1958 to 1997 were analyzed, the changes were studied by decade, and the results were compared with other Japanese studies and reports from other countries. The autopsy cases in the Annual⁹⁾ were in good correspondence with the Japanese mortality statistics⁵⁾ and had a high percentage of accurate histological data (99.13% for 1997). The characteristics of

lung cancer in Japan, and the recent changes and likely future of lung cancer in North America, Europe and Asian countries are discussed.

MATERIALS AND METHODS

All the lung cancer cases consecutively registered in the Annual of Autopsy Cases in Japan⁹⁾ over the 40-year period from 1958 to 1997 were reviewed individually and analyzed. Cases such as latent lung cancer, not the cause of death clinically or pathologically, and those which were cured or in remission due to surgery and/or radiotherapy were not counted as lung cancer. They were divided into four chronological groups (periods I to IV) according to decade. The non-specific term for histological type “anaplastic carcinoma” was often used in the Annual until the 1970s, and necessitated its use here. The registration rates in the Annual, compared with the total deaths, all malignancies and lung cancer cases in Japan for each 5-year period in the study were referenced against the Japanese mortality statistics.⁵⁾ From the Annual,⁹⁾ the frequency of malignant tumors and lung cancer cases among all autopsy cases, that of lung cancer in the malignant autopsy cases, the relative incidences of other major malignancies, the

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histological and age distributions of patients with lung cancer for each of the four periods, the male-to-female ratios by age group and the four major histological types were studied.

The statistical significance of time trends in the histological distribution for both sexes, the male-versus-female ratio in periods III and IV and the total for the major histological types, was determined using the χ^2 test. The histological types of lung cancer by age group and chronological period, and the significance of mean age values among the periods was analyzed using the standard error method. The criterion of statistical significance was $P < 0.05$.

RESULTS

Background of the Annual, compared with the Japanese mortality statistics

Male/female ratios of lung cancer in the mortality statistics (Fig. 1): The total autopsy cases in the Annual per total deaths in Japan increased to 6.3% in 1985 and decreased to 3.0% in 1997. The total malignant cases in the Annual per total malignant deaths in Japan increased to 12.5% in 1980 and decreased to 5.8% in 1997. The lung cancer cases in the Annual per total of lung cancer deaths in Japan increased to 14.0% in 1980 and decreased to 5.2% in 1997.

The male-to-female ratio for lung cancer in the Japanese mortality statistics was 2.3 in 1965, increased to 2.8 in 1990, and was 2.7 in 1995 and 1997.

Incidence of lung cancer in the Annual (Fig. 2): The absolute number of lung cancer cases increased until period III,

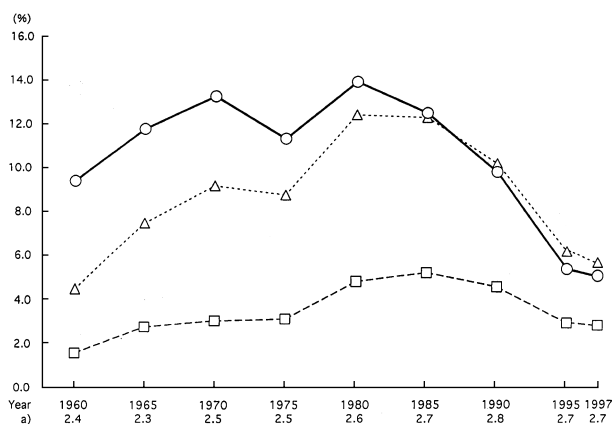


Fig. 1. Background of the annual Japanese mortality statistics and male/female ratio of lung cancer cases (Annual of Autopsy Cases in Japan 1958–97). a) M/F ratio of lung cancer^{b)} cases of mortality statistics. b) Cancer of the trachea, bronchus and lung (ICD 9th revision: 162). O., autopsy rate of lung cancer cases; Δ, autopsy rate of malignant cases; □, total autopsy rate.

but decreased in period IV in both sexes. The male-to-female ratio of lung cancer increased from 2.8 in period II to 3.5 in period IV. Malignant tumor cases at autopsy increased and were more than 60% in males from period III and more than 50% in females from period II, but decreased slightly in females between periods III and IV. Lung cancer cases in the malignant tumor cases increased in both sexes and were nearly 20% for males from period IV and more than 10% for females from period III. Lung cancer cases at autopsy increased for both sexes, and were more than 10% in males from period III, and more than 5% in females from period III.

Five most frequent malignant tumors by decade (Figs. 3 and 4): In males, gastric cancer was the most frequent

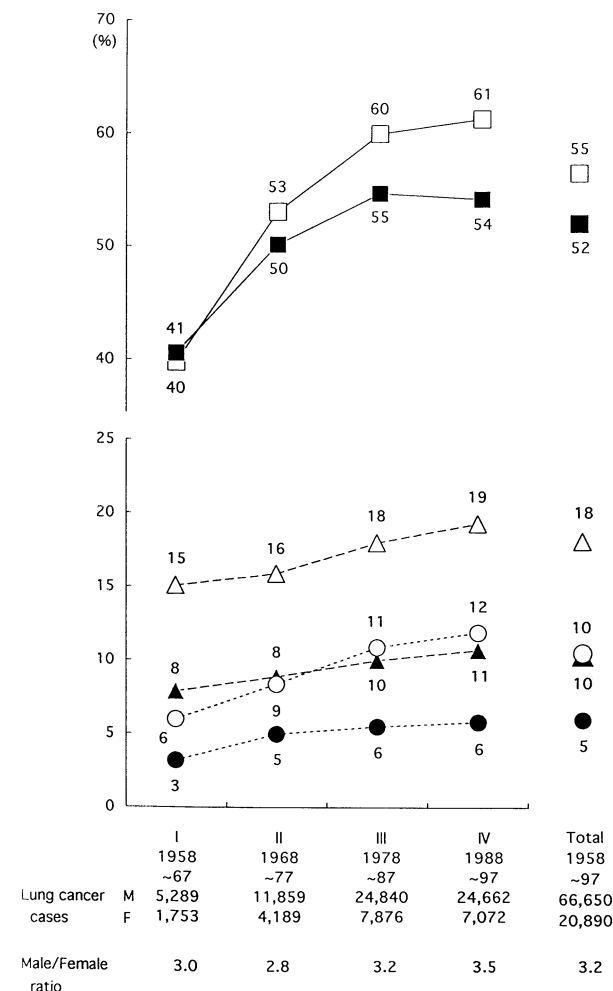


Fig. 2. Incidence of lung cancer cases (male and female) at autopsy (Annual of Pathological Autopsy Cases in Japan 1958–97). □ M, ■ F, malignant tumor cases at autopsy (%); Δ M, ▲ F, lung cancer cases among malignant tumor cases (%); ○ M, ● F, lung cancer cases at autopsy (%).

tumor until period II, but was surpassed by lung cancer from period III. Gastric cancer decreased from 24.9% to 15.8% during the study period. Lung cancer increased from 15.2% to 19.3% from period I to IV. Liver cell carcinoma also gradually increased.

In females, gastric cancer was the most frequent tumor during the study period, but the incidence gradually decreased from 20.7% to 12.6%. Lung cancer gradually

increased from 8.0% to 10.7%, and became the second most frequent tumor in periods III and IV.

Changes in the histological distribution of lung cancer (Figs. 5 and 6): Adenocarcinoma was the most frequent, and squamous cell carcinoma was the next most frequent type in both sexes for all periods. In males, adenocarcinoma increases from period II to IV, and the increase was significant between periods III and IV. Squamous cell carcinoma decreased from period II to IV, and the decreases were significant between periods II and III, and III and IV. Small cell carcinoma accounted for 19% and 8% in periods III and IV, respectively. In periods I and II, anaplastic carcinoma accounted for more than 10% and markedly decreased in period III to 2%.

In females, adenocarcinoma increased from period II to IV, and the increases were significant between periods II and III, and III and IV. Squamous cell carcinoma decreased from period II to IV, and the decreases were significant between periods II and III, and III and IV. Small cell carcinoma accounted for 15% and 14% and large cell carcinoma for 7% and 6% in periods III and IV, respectively. Anaplastic carcinoma accounted for around 10% in

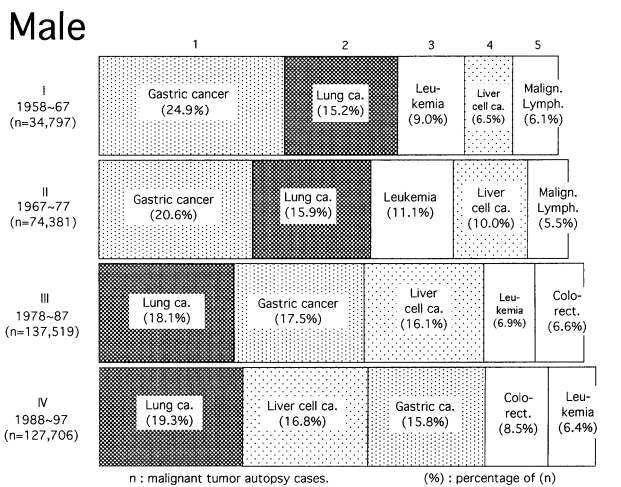


Fig. 3. Five most frequent malignant tumors among autopsy cases by decade (Annual of Pathological Autopsy Cases in Japan 1958-97). n: malignant tumor autopsy cases. (%): percentage of (n).

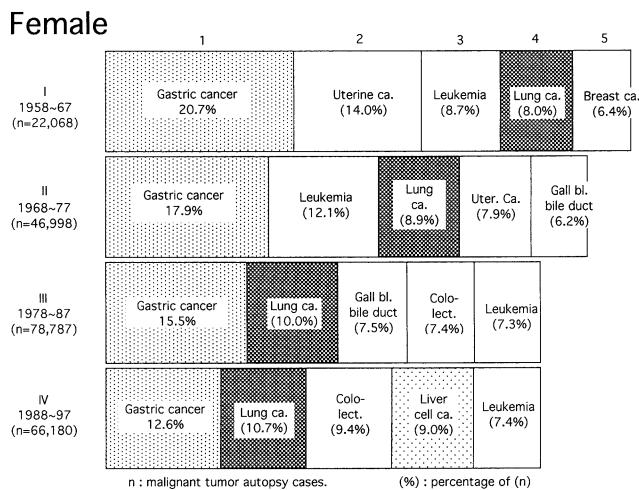


Fig. 4. Five most frequent malignant tumors among autopsy cases by decade (Annual of Pathological Autopsy Cases in Japan 1958-97). n: malignant tumor autopsy cases. (%): percentage of (n).

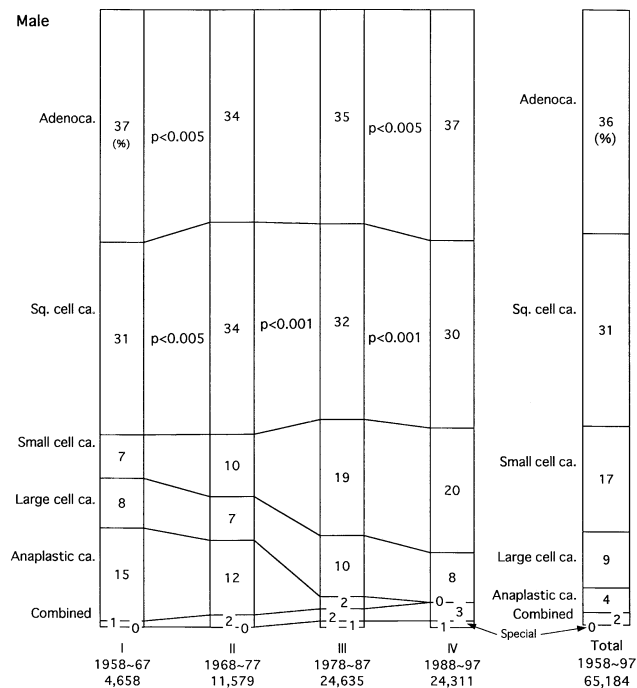


Fig. 5. Changes in the histological distribution of lung cancer (Annual of Pathological Autopsy Cases in Japan 1958-97). Significance for time trends: Adenocarcinoma. I>II ($P<0.005$), III<IV ($P<0.005$); Squamous cell carcinoma. I<II ($P<0.005$), II<III ($P<0.001$), III<IV ($P<0.001$).

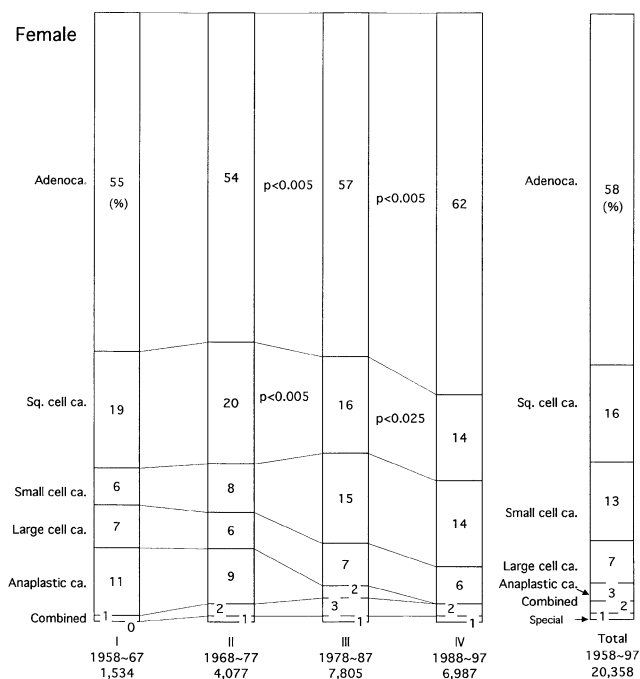


Fig. 6. Changes in histological distribution of lung cancer (Annual of Pathological Autopsy Cases in Japan 1958-97). Significance for time trends: Adenoca. II<III ($P<0.005$), III<IV ($P<0.01$); Sq. cell ca. II>III ($P<0.005$), III>IV ($P<0.001$). Significance for time trends in female: Adenoca. II<III ($P<0.005$), III<IV ($P<0.005$); Sq. cell ca. II>III ($P<0.005$), III>IV ($P<0.025$). Significance for male vs. female (periods III, IV and Total)—Adenoca.: Male<Female ($P<0.005$); Sq. cell ca., Small cell ca. and Large cell ca.: Male>Female ($P<0.005$).

periods I and II, but decreased to 2% and 0% in periods III and IV, respectively.

In periods III, IV and the total, adenocarcinoma was significantly more frequent in females, and squamous cell carcinoma, small cell carcinoma and large cell carcinoma were significantly more frequent in males than in females.

Distribution of major histological types of lung cancer cases by age group and chronological period (Tables I and II): The peak age shifted from the 60s to the 70s in the total, squamous cell carcinoma and small cell carcinoma in both sexes and in female adenocarcinoma. In male adenocarcinoma, the peak shifted from the 60s to the 70s between periods II to III, but moved back to the 60s in period IV. For large cell carcinoma in males, the peak was the 60s during the study period, but in females it shifted from the 50s to the 70s.

The mean ages rose from around 60 years to 70 years during the study period, and the rises between decades were significant for the four major histological types and the total in both sexes, except for one case each of large cell carcinoma in both sexes.

Male-to-female ratios of lung cancer by the four major histological types and age group (Fig. 7): The curves of male-to-female ratios increased the 10s or 20s to the 50s or 60s and gradually decreased until the 90s in the total and the four major histological types. The highest curve was for squamous cell carcinoma, followed by small cell carcinoma and then large cell carcinoma. The curve for the total was fourth and adenocarcinoma showed the lowest curve.

DISCUSSION

The Japanese mortality statistics⁵ include no histological data on lung cancer cases. In a population-based study,¹⁰ the number of cases with histological diagnosis was insufficient. Clinical studies use biopsies and cytological results as histological data. They are sometimes not representative of tumors of several centimeters in size and are often not the final histological diagnosis. In pathological autopsy cases, approximately 40% of clinical diagnostic errors were observed in cancer cases,¹¹ and major clinical diagnoses were erroneous in around 10% of cases in the 1960, 1970, and 1980.¹² Surgery is done on the basis of indication for operation and extensive disease is first excluded. Autopsy cases have their own bias, as the total includes advanced and/or fatal cases, and the autopsy rate is low and gradually decreasing worldwide. In the United States, shortly after World War II, nearly 50% of death were autopsied.¹³ Autopsies for non-medicolegal deaths in the United States declined from 13% in 1980 to 10% in 1985.¹⁴

The population-based study¹⁵ clarified the death rate and incidence of lung cancer, which were 1.18 (1978-80) and 1.20 (1984-86).¹⁵ The results showed that lung cancer is a highly malignant entity with few opportunities for significant therapeutic effects, and also delineate the approximate relationship between mortality statistics, autopsies and clinical cases.

The Japanese mortality statistics⁵ classify neoplasms of the trachea and the lung together. The author's previous autopsy studies^{16, 17} clarified the relative incidence of tracheal cancer and lung cancer,¹⁶ and that of lung sarcoma and lung cancer.¹⁷ These results showed that 99.3% for males and 99.0% for females of trachea, bronchus and lung neoplasm consisted of lung cancer.

Although male lung cancer has declined since the 1970s in the United States^{1, 2} and several European countries,¹⁸ the Japanese mortality statistics^{5, 6} and this study have shown a continuous increase since the 1950s.

For the histological classification of lung cancer, most Japanese pathologists use both the World Health Organization's (WHO) International Histological Classification of Lung Tumours¹⁹ and the Japanese Lung Cancer Society's Classification of Lung Cancer,^{20, 21} which are essentially

Table I. Histological Types of Lung Cancer Autopsy Cases (Male) by Age Group and Chronological Period (Annual of Pathological Autopsy Cases in Japan 1958–67, 1968–77, 1978–87 and 1988–97)

Histological type	Age group	–9	10–	20–	30–	40–	50–	60–	70–	80–	90–	Total cases	Mean±SD	
All histol. types	1958–67	2	10	53	192	498	<u>1438</u>	2034	938	93	8	5266	60.9±11.4	*3
	1968–77	2	8	70	286	972	2175	4543	<u>3311</u>	476	6	11849	64.1±11.3	
	1978–87	1	4	47	348	1343	4336	<u>7740</u>	8874	2066	73	24832	67.0±11.0	*3
	1988–97	0	3	25	193	1143	3203	<u>8209</u>	8541	3031	164	24512	68.6±10.9	
Adenoca.	1958–67	1	3	22	86	217	<u>500</u>	623	258	24	1	1735	59.3±13.0	*2
	1968–77	1	4	30	142	391	760	1448	<u>1021</u>	157	4	3958	63.1±12.1	
	1978–87	0	2	22	198	611	1663	<u>2603</u>	2722	654	27	8502	65.1±11.8	*2
	1988–97	0	2	12	101	587	1407	3085	<u>2868</u>	1006	70	9138	67.4±11.4	
Sq. cell ca.	1958–67	0	0	4	30	96	<u>344</u>	627	313	29	4	1447	63.2±10.1	*2
	1968–77	1	2	8	50	234	677	1541	<u>1206</u>	174	1	3894	65.5±10.4	
	1978–87	0	0	3	41	252	1111	<u>2314</u>	3256	785	22	7784	69.0±10.8	*3
	1988–97	0	0	3	21	161	719	<u>2352</u>	2937	1093	47	7333	70.7±9.8	
Small cell ca.	1958–67	0	2	8	16	26	<u>103</u>	123	60	2	0	340	59.7±12.4	*2
	1968–77	0	0	7	31	106	220	471	<u>344</u>	30	0	1209	63.8±11.0	
	1978–87	0	1	9	36	228	853	<u>1558</u>	1652	358	12	4707	67.0±10.6	*3
	1988–97	0	1	6	24	170	618	<u>1744</u>	1771	562	30	4926	68.9±10.2	
Large cell ca.	1958–67	1	0	6	18	39	<u>100</u>	123	64	8	0	359	59.9±12.4	*3
	1968–77	0	0	7	14	76	152	343	<u>230</u>	30	1	853	65.8±11.1	
	1978–87	0	0	5	52	161	484	785	<u>770</u>	174	8	2439	65.7±11.5	NS
	1988–97	0	0	0	35	172	317	704	<u>611</u>	211	9	2059	66.4±11.7	

Bold-face numbers are the most frequent and underlined numbers are the next most frequent case numbers in each chronological period. Significance of mean age values for time trends. *1: $P < 0.05$, *2: $P < 0.01$, *3: $P < 0.001$.

similar, especially in the four major histological types. The latter^{20, 21)} is becoming more similar to the former¹⁹⁾ with the publication of new editions. The main difference is that solid adenocarcinoma with mucin in the WHO¹⁹⁾ is termed mucus-producing large cell carcinoma in the Japanese Classification.²¹⁾ The Japanese Classification²¹⁾ states that in principle, large cell carcinoma is only assigned to cases in which large cell can be recognized. Practically, the percentages of large cell carcinoma in this study, less than 10% in both sexes, are reasonable. The disappearance of the term “anaplastic carcinoma” since period III has made for better comparability with other reports.

In Japanese, lung cancer includes a high percentage of adenocarcinoma in both sexes, and this was also found to be the case in autopsy studies.^{7, 8)} But in males, squamous cell carcinoma was the most frequent, and adenocarcinoma was the second most frequent in clinical²²⁾ and pop-

ulation-based cases,¹⁰⁾ as well as surgical cases diagnosed by the author.²³⁾

In a population-based study in the United States for males (1973–87), Travis *et al.*¹⁾ noted a slight increase or no change in squamous cell carcinoma, and a rapid increase in adenocarcinoma, while squamous cell carcinoma (36%) was the most frequent, followed by adenocarcinoma (26%). In contrast Thun's results²⁾ showed that adenocarcinoma surpassed squamous cell carcinoma between 1990 and 1991. Although adenocarcinoma in females was the most frequent (37%) in Travis' paper,¹⁾ it was much lower than in this study.

In Europe, while squamous cell carcinoma is the most frequent in males in many countries, in the Netherlands,³⁾ Denmark⁴⁾ and youngest cohort in Strasbourg,²⁴⁾ adenocarcinoma has begun to increase. In recent years in Denmark (1978–94),⁴⁾ squamous cell carcinoma markedly decreased

Table II. Histological Types of Lung Cancer Autopsy Cases (Female) by Age Group and Chronological Period (Annual of Pathological Autopsy Cases in Japan 1958–67, 1968–77, 1978–87 and 1988–97)

Histological type	Age group	-9	10-	20-	30-	40-	50-	60-	70-	80-	90-	100-	Total cases	Mean±SD	
All histol. types	1958–67	0	4	36	102	266	<u>467</u>	555	268	47	5		1750	58.8±12.9	*3
	1968–77	1	7	37	174	476	923	1344	<u>1018</u>	191	11		4182	62.2±12.7	
	1978–87	0	5	31	205	588	1335	<u>2259</u>	2615	786	50		7874	65.2±12.5	*3
	1988–97	0	3	17	100	475	936	<u>1899</u>	2375	1112	102	6	7025	68.8±12.5	
Adenoca.	1958–67	0	1	15	58	143	<u>238</u>	241	121	20	2		839	57.9±12.9	*3
	1968–77	0	2	20	106	264	<u>552</u>	687	491	82	6		2210	61.3±12.6	
	1978–87	0	1	19	146	424	882	<u>1238</u>	1328	414	28		4480	64.8±12.9	*3
	1988–97	0	2	12	78	354	671	<u>1222</u>	1266	646	68	5	4324	67.6±13.0	
Sq. cell ca.	1958–67	0	0	0	5	36	<u>74</u>	100	60	13	2		290	62.6±11.4	*1
	1968–77	0	0	1	25	82	146	244	<u>238</u>	59	2		797	64.7±12.3	
	1978–87	0	3	1	13	43	134	<u>365</u>	506	164	11		1240	69.8±11.0	*3
	1988–97	0	0	2	4	36	76	209	429	<u>216</u>	19		991	72.6±10.9	
Small cell ca.	1958–67	0	0	3	8	8	<u>23</u>	30	19	0	0		91	58.8±13.2	*2
	1968–77	1	2	6	8	32	54	126	<u>95</u>	11	0		335	63.1±13.0	
	1978–87	0	1	5	18	36	154	<u>360</u>	449	112	5		1140	68.4±11.0	*3
	1988–97	0	0	2	9	31	87	<u>287</u>	439	131	7		993	71.4±10.7	
Large cell ca.	1958–67	0	0	5	6	19	34	<u>30</u>	15	3	0		112	57.1±13.4	*2
	1968–77	0	1	3	10	27	52	77	<u>58</u>	12	0		240	62.0±13.1	
	1978–87	0	0	2	17	45	86	<u>167</u>	202	48	5		572	66.4±12.4	*3
	1988–97	0	0	0	6	34	67	<u>103</u>	142	76	5		433	68.6±12.6	

Bold-face numbers are the most frequent and underlined numbers are the next most frequent case numbers in each chronological period. Significance of mean age values for time trends. *1: $P < 0.02$, *2: $P < 0.01$, *3: $P < 0.001$.

(43%) and adenocarcinoma increased (23%) in males. Adenocarcinoma in females⁴⁾ also increased and was the most frequent, but the percentage was low (39%).

In Korean clinical cases in males,²⁵⁾ squamous cell carcinoma accounted for more than half (54%) and adenocarcinoma was low (18%), while in females adenocarcinoma was the most frequent, though still less than half (45%), and squamous cell carcinoma was rather high (28%).

In China,²⁶⁾ lung cancer has gradually increased in both sexes (1980–89). Among clinical cases in males²⁷⁾ squamous cell carcinoma was the most frequent, but decreased from 68% to 53%, and adenocarcinoma increased from 14% to 27%. In females, adenocarcinoma decreased from 64% to 39%, and squamous cell carcinoma increased from 22% to 32%.

In the Japanese mortality statistics (1950–95),⁶⁾ the peak age in both sexes has gradually shifted to more than

85 years old. The average age of death in 1995 was 71.6 years for males and 73.0 years for females.

In clinical cases, the peak ages are lower than in autopsy studies. In Korea,^{26, 28)} these were in the 60s for both sexes. In the United States,²⁹⁾ for the three major histological types other than large cell carcinoma, these were all between 55 and 64 years.

Concerning the male-to-female ratio of lung cancer, the author^{7, 8)} noted that the curves of mortality rates by age group in each county³⁰⁾ show good compatibility with the histological distribution of lung cancer. In the 1960s, the curves for United States, France, and England,³⁰⁾ with high percentages of squamous cell carcinoma and small cell carcinoma, were high and that of Japan,³⁰⁾ with a high percentage of adenocarcinoma, was low. The ratio in the United States then markedly decreased to 1.9 (1990–91),²⁾ in accordance with the decrease in the smoking rate, espe-

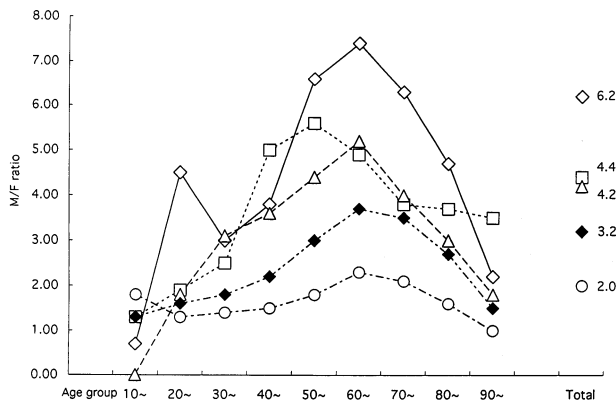


Fig. 7. Male/female ratio of lung cancer by age group (Annual of Pathological Autopsy Cases in Japan 1958–97). \diamond , Sq. cell ca.; \square , Small cell ca.; \triangle , Large cell ca.; \blacklozenge , Total; \circ , Adenoca.

cially in males, and a reversion of squamous cell carcinoma to adenocarcinoma was seen around 1990.²⁾ The ratio in Montreal clinical cases was just 2.0 in 1993.

In Europe the ratio is still high: 12 in Strasbourg in 1993,²⁴⁾ and 10.0 in Bohemia (1981–85).³¹⁾ Parallel with the decrease in cigarette consumption, the lung cancer mortality rates in England-Wales and Switzerland³²⁾ have decreased. The ratio in Denmark in 1993–94 was 1.6,⁴⁾ and since 1983 squamous cell carcinoma and small cell carcinoma have decreased and adenocarcinoma has increased. Although there has been a marked decrease in the percentages of male smokers in some European countries,^{3,4)} that of females is still around 40%.

The ratio in Asia is low. The ratio was 2.6 in the Philippines in 1990–1991,³³⁾ 2.1 in China²⁶⁾ in 1979, and 2.7 in Japan in 1997.⁵⁾ The smoking rates for lung cancer cases in Asian women are low. They were 18% in Korea (1981–90),²⁵⁾ 38% in the Philippines (1981–88),³³⁾ and 31% in the author's cases (1976–91).³⁴⁾ Smoking prevalence in the United States from 1965 to 1991²⁹⁾ markedly decreased from 50% to 30% in males, and from 35% to 25% in females. The current similarity in percentages between both sexes is surprising,²⁹⁾ but the percentage in females is higher than that in Japan (13.7% in 2000).³⁵⁾ The percentage of those who have never smoked among lung cancer patients is less than 10%,³⁶⁾ except for female bronchiolar alveolar carcinoma. In the author's own experience, the percentages of female adenocarcinoma in autopsy cases were 71.8%³⁷⁾ and 78.6%.³⁴⁾ In clinical cases in the Philippines,³³⁾ the percentage was 70.4%. The author has published data³⁴⁾ on male adenocarcinoma cases, in which non-smokers were significantly more differentiated than smokers. In case distribution by degree of differentiation of female adenocarcinoma,³⁷⁾ non-smokers were more sig-

nificantly well-differentiated type-predominant, according to the number smoked per day. In female well-differentiated adenocarcinoma, non-smokers amounted to 80.5%³⁷⁾ and 86.4%.³⁴⁾ There may be an essential difference in female adenocarcinoma between the United States²⁹⁾ with high smoking rates, and Asia³³⁾ and Japan.³⁵⁾ It seems likely that female adenocarcinoma in the United States is more poorly-differentiated subtype-predominant. The cause of well-differentiated adenocarcinoma in non-smoking Asian females^{33,34,37)} is at present unknown.

As mentioned previously, the Annual⁹⁾ contains histological data on lung cancer, and shows good correspondence with the Japanese mortality statistics^{5,6)} in terms of absolute and relative increases, age distribution, upward shift of mean ages, and male-to-female ratios and their changes. Lung cancer in Asian countries has many common points in its patterns of increase, histological distribution, male-to-female ratios, and smoking rates.

From the male-to-female ratios of lung cancer and the status of smoking habits, lung cancer in the world at present can be divided into three groups:

1) Group A (North American type), including the United States,^{1,2)} Canada,²⁴⁾ and some European countries.^{3,4)} In this group, effective anti-smoking policies, especially in men, and the effects of the introduction of low-nicotine and low-tar cigarettes,³⁸⁾ have caused a marked drop in the male-to-female ratio to around 2.0.^{2,24)} The smoking rate in women is around 25% to 30%.²⁹⁾ A switch of squamous cell carcinoma to adenocarcinoma in men has been observed.^{2,38)}

2) Group B (European type), in which consumption of cigarettes is still increasing.³²⁾ There is a high male-to-female ratio of around 8 to 10,³¹⁾ and high percentages of squamous cell carcinoma and small cell carcinoma in men.³⁾ Adenocarcinoma in women is the most frequent type, though less than 40%.⁴⁾ and the smoking rate in women is high (40%).⁴⁾ In countries with successful anti-smoking policies,³²⁾ a transition to Group A has been seen.

3) Group C (Asian type) shows a low male-to-female ratio of around 3.0. There is typically a rather high smoking rate in men (from 84% in 1968 to 53.5% in 2000, Japan),³⁵⁾ but a low percentage in women (from 18% in 1966 to 13.7% in 2000, Japan).³⁵⁾ In both sexes, adenocarcinoma is the most frequent type in autopsy cases.^{7,8)} Well-differentiated papillary adenocarcinoma in non-smoking women is typically high.^{34,37)} Owing to an increasing smoking rate in Japanese females in their 20s (10% in 1970 to 21.9% in 2000),³⁵⁾ an increase in the American type non well-differentiated adenocarcinoma in this cohort is to be expected in the near future. With more effective anti-smoking policies, especially in Group C men and Group A women, Group C and Group A could converge in future decades.

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