

# Lung cancer in Hong Kong Chinese: Mortality and histological types, 1973-1982

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**Summary** The histological types of lung cancer in Hong Kong Chinese in both sexes are presented. When the 1981 WHO Classification is used instead of the 1967 WHO Classification, more than half of the large cell carcinoma is retyped into the adenocarcinoma group. The proportion of large cell carcinoma thus decreases from 14.7% to 6.9% in the male and from 10.0% to 4.4% in the female. Compared to the 1948-1962 report from the same Department, there is a shift of the peak age distribution from the 6th decade to the 7th decade. Compared to the 1960-1972 report from the same Department, there is a significant increase in the relative frequency of adenocarcinoma in both sexes, from 15.6% to 25.8% in the male and 34.3% to 49.6% in the female. Adenocarcinoma continues to be the most common histological type in females and it is becoming the commonest type in males. It is also found in the present series that in the male, the proportion of adenocarcinoma decreases with increasing age, from 60% in the third decade to 26.6% in the eighth decade. In spite of the high female lung cancer mortality rate and therefore low male:female ratio of about 2:1, there is a tendency for this ratio to increase over the years. It is speculated that factors other than active cigarette smoking may be responsible for the peculiar and changing histological pattern and the female predominance in lung cancer in Hong Kong Chinese.

Since the late 1960s, when lung cancer replaced liver cancer as the most important cause of cancer death in Hong Kong, there has been a steady increase in mortality from this malignancy in both sexes throughout the last 15 years. The mortality rate on 1981 of 53.3 in the male and 22.9 in the female is more than double that of 21.7 and 11.4 in 1960 respectively (age-adjusted to world standard population, Waterhouse *et al.*, 1976).

Lung cancer in Hong Kong Chinese is peculiar in that there is a high incidence in females, a fact shared by Chinese populations in other parts of the world, including China, Singapore, California and Hawaii (China, 1979; Law *et al.*, 1976; Waterhouse *et al.*, 1976). This results in a very low male:female ratio of about 2:1. In addition, the proportion of adenocarcinoma among females is high.

Material from the same department has been reported in two separate articles, covering the periods 1948-1962 and 1960-1972 respectively (Lee & T'so, 1963; Chan & MacLennan, 1977). This present study reviews the histological types of lung cancer in the period 1973-1982 and draws attention to the changing histopathological pattern and age and sex incidence over the last two decades in Hong Kong. A comparison is also made of the percentage distributions of the various histological types using the two WHO Classifications, (WHO, 1967; WHO, 1981).

The present series is the largest series of lung cancer cases in Hong Kong ever reported. The observation of the difference in distribution in cell types when using the 1967 and 1981 WHO classification is also reported for the first time in Hong Kong.

## Materials and methods

All bronchial and lung cancer cases in the 10-year period 1973-1982 from the University Department of Pathology, Queen Mary Hospital were reviewed. Rare lung tumours such as carcinoids, adenoid cystic carcinoma, mucoepidermoid tumour, sarcomas and metastatic carcinoma were all excluded from this study. The tissues came from surgery and autopsy. Only Chinese patients were included.

Surgical material included bronchial biopsies, transbronchial lung biopsies, needle biopsies, and resection specimens. Biopsies of lymph nodes alone were not included. The majority of the specimens came from the thoracic units of medical and surgical departments of the Queen Mary Hospital which is the major general hospital of Hong Kong Island, and from the Grantham Hospital which is a cardiothoracic centre. A minority of specimens came from private clinics.

Rigid bronchoscopy was the chief method for obtaining biopsies before 1978. Since then this was substantially replaced by fiberoptic bronchoscopy

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which allowed both bronchial and transbronchial lung biopsies. Patients with both biopsy and resection were included in the resection series.

Autopsy material covered all necropsies on lung cancer cases during the period in the Queen Mary Hospital, except those performed for medical-legal purposes. Cases that appeared in both the surgical and the autopsy series were included in the analysis of the surgical (resection) series, so that all the cases were analysed chronologically according to the year of diagnosis.

All the original histological sections were reviewed, with no knowledge of sex, age of the patients and the reported diagnoses. Histological typing was based on WHO International Histological Typing of Lung Tumours. Both the 1967 and 1981 classifications were used simultaneously. The criteria were strictly followed and adopted by both of the pathologists (ITMK & KFS). Whenever there was a suggestion that the tumour could be an adenocarcinoma, Alcian Blue and Periodic Acid Schiff stains were performed for identification of both acid and neutral mucin.

The tumours were grouped into the four major types, i.e. squamous cell (epidermoid) carcinoma, small cell (anaplastic) carcinoma, adenocarcinoma, and large cell carcinoma. No subtyping was attempted, and bronchiolo-alveolar carcinoma was included in the adenocarcinoma group. There were four cases of combined squamous and adenocarcinoma, two in either sexes. They were grouped under the heading "Others". Biopsies, mainly transbronchial ones, that were adequate for diagnosis of malignancy but insufficient for typing were also put into the "Others" group.

Cases without histological examination of the primary tumour of the lungs, or were diagnosed by cytology alone were excluded from the series.

## Results

There were 636 biopsies, 175 resection specimens and 263 autopsies. Nineteen of the autopsy cases appeared in both the surgical and the autopsy series, and were included in the analysis of the resection series. The rest of the autopsy cases had no biopsy or ante-mortem medical or surgical treatment. There is thus a total of 1055 cases: 714 males and 341 females. The three sources of tissue were combined for analysis of the percentage distribution of histological types, as this should reflect better the overall picture in life. The histological types by year and sex are presented in Table I.

When the 1981 WHO Classification is used instead of the 1967 Classification, the percentage of

adenocarcinoma in males is increased from 25.8 to 33.6 and in females from 49.6 to 55.1. This increase is due to reclassification of 53.3% and 55.9% of the cases in the male and female respectively from being classified as Type IV according to the 1967 Classification to Type 3 according to the 1981 Classification. The main difference between the two classifications in this respect is the inclusion of solid large cell carcinoma with mucin secretion into the adenocarcinoma group in the 1981 Classification. The figures for epidermoid (squamous) carcinoma and small cell (anaplastic) carcinoma remain the same in both classifications.

The sex and age distribution of all 1055 cases of lung cancer irrespective of type is shown in Figure 1. The largest number of cases occurs in the 7th decade, followed by the 6th decade in the male and the 8th in the female. The overall male:female ratio is 2.1:1. The male:female ratio is higher than 2.1:1 in and before the 7th decade and is highest in the 6th (3.5:1). After the 7th decade, the ratio diminishes and is less than 1 in the 9th decade and after.

The mean age of male patients is 60.5 years and that of female patients 64.4. Using the WHO 1981 Classification, the mean ages of males in years in the four main types are: 61.3, in squamous carcinoma; 62.8, in small cell carcinoma; 58.4, in adenocarcinoma; 60.6, in large cell carcinoma. Those in females are 64.8; 67.8; 63.6; and 63.0 respectively.

The percentage distribution of histological type by age group and sex is shown in Table II. In males, there is a trend for the proportion of adenocarcinoma to decrease with age. In females however, the trend is not obvious.

## Discussion

As in many Occidental countries, there has been a steady increase in the incidence and mortality rate of lung cancer in Hong Kong over the last twenty years. Despite the influx of immigrants from Mainland China, (which are usually young males), the total number of lung cancer cases and of lung cancer deaths as well as mortality rates (crude or age adjusted) have been increasing. The increasing rates are due to the greater increase in the total number of lung cancer deaths than the increase in population. The increasing trend is also reflected in the present series. There was a 60% increase in the average number of cases per annum in both sexes when compared with the series by Chan & MacLennan (1977), covering the period 1960-1972.

Compared to Occidental countries, the incidence in males is not striking. Hong Kong ranks only

**Table I** Percentage distribution by sex of histological types of lung cancer. Necropsy and surgical material combined in University Department of Pathology, Hong Kong Island, 1973-1982.

Year	Male					Female					Total number
	I (1)	II (2)	III (3)	IV (4)	Others	I (1)	II (2)	III (3)	IV (4)	Others	
1973	26.9	25.4	19.4	20.9	7.5	25.0	15.0	42.5	12.5	5.0	40
1974	31.0	22.4	22.4	19.0	5.2	15.8	31.6	31.6	21.0	0	19
1975	41.7	14.6	31.3	12.5	0	18.2	9.1	68.2	4.5	0	22
1976	27.0	37.8	27.0	5.4	0	15.8	15.8	47.4	15.8	5.0	19
1977	27.5	20.0	37.5	12.5	2.5	40	7.4	40.7	18.5	7.4	27
1978	34.3	16.4	22.4	19.4	7.5	16.1	16.1	48.4	16.1	3.2	31
1979	51.1	16.3	18.5	8.7	5.4	26.7	4.4	46.7	13.3	8.9	45
1980	38.4	18.2	25.2	12.1	6.1	30.4	13.0	47.8	2.2	6.5	46
1981	26.8	19.6	34.0	11.3	8.2	28.3	15.2	45.7	4.4	6.5	46
1982	24.8	27.5	25.7	21.8	0.92	13.0	8.7	69.6	4.4	4.4	46
Total	33.3	21.3	25.8	14.7	4.9	22.6	12.6	49.6	10.0	5.3	341
Total <sup>a</sup>	43.6	21.5	15.6	15.8	3.5	22.7	23.8	34.3	16.2	2.9	277

Type I (1): Epidermoid (squamous) carcinoma;

Type II (2): Small cell (anaplastic) carcinoma;

Type III (3): Adenocarcinoma;

Type IV (4): Large cell carcinoma;

Others includes combined epidermoid and adenocarcinoma (adeno squamous carcinoma) and unclassifiable carcinomas. Roman numerals represent the 1967 and Arabic the 1981 WHO classification. Since the percentages for squamous and adenocarcinomas are the same in both classifications, only one column of figure is presented.

<sup>a</sup>Figures from 1960-1972 for comparison (Chan & MacLennan, 1977).

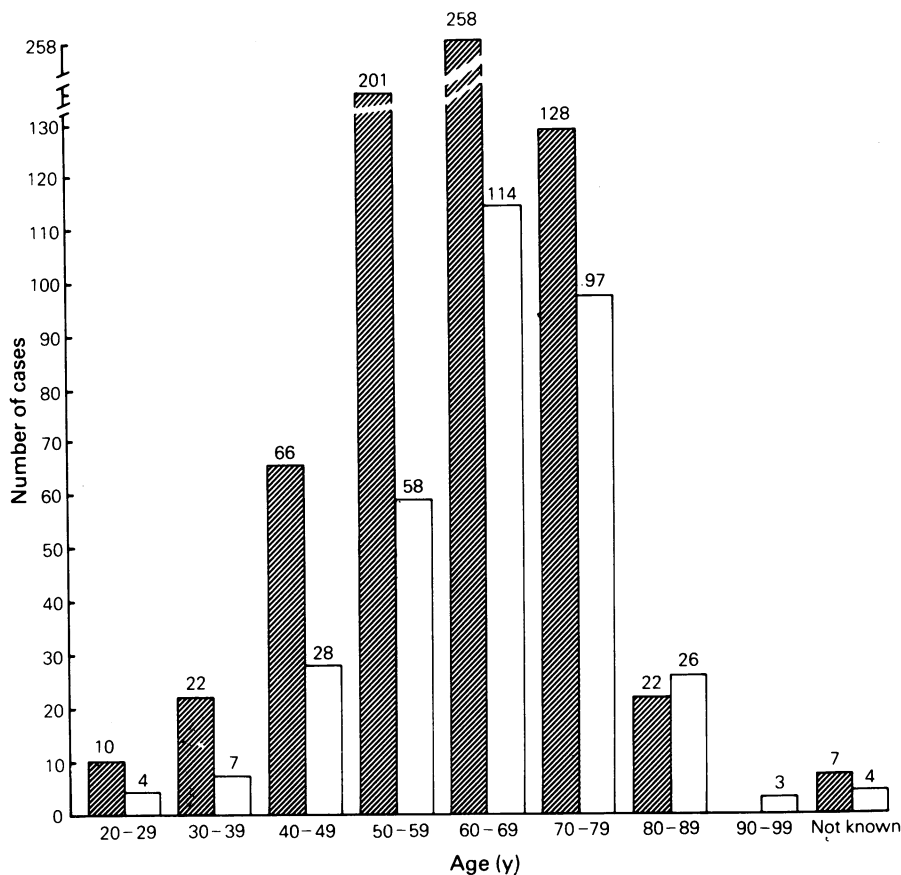


Figure 1 Sex and age distribution of 1055 cases of lung cancer irrespective of type. (▨) male; (□) female.

twenty-first in male lung cancer mortality in the world in 1975 (Segi *et al.*, 1981). The more notable feature is in the female. The mortality in Hong Kong Chinese female is highest in the world (Segi *et al.*, 1981), possibly second only to the Maoris in New Zealand (Waterhouse *et al.*, 1976). This results in the strikingly low male to female ratio which is about 2:1. In Occidental countries, the male:female ratio has been high. In 1960, the ratio in Scotland and USA were 7.6 and 6.6, respectively (Segi *et al.*, 1981). Since then there has been a decrease in this ratio as lung cancer in the female gain more importance. In Hong Kong, although the male:female ratio has been outstandingly low, there is a tendency to increase instead of the contrary. The ratio calculated from mortality rates, was 1:1 in 1960 and has increased through 1.5 in 1972 to 1.8 in 1981 (Hong Kong, 1960-1981). This gradual increase in male:female ratio is reminiscent of the trend before 1960 in European countries and the United States. This is perhaps because cigarette

smoking has not really become popular until after the Second World War for economic reasons.

The male:female ratio for the period 1973-1977 in the present series is 1.96:1 and that for 1978-1982 is 2.17:1. This series thus also reflects the trend in the whole population. It is also interesting to note that in Japan there is also a tendency for the male:female ratio to increase in recent years (Segi *et al.*, 1981).

In the present paper, we hope to reflect the changes in histological types in Hong Kong by studying material in our Department collected at different times. It may be argued that results from one department may not be representative of the whole colony. However, while proportional distribution in lung cancer cell types and its secular trend should ideally be studied on series derived from population-based cancer registry, it is not practicable in Hong Kong because more than half of the lung cancer cases notified (voluntarily) to the registry were not confirmed histologically. Data on

Table II Percentage distribution of histological type by sex and age group, WHO 1967 (WHO 1981) classification.

Age group	Male					Female						
	I (1)	II (2)	III (3)	IV (4)	Others	Total number	I (1)	II (2)	III (3)	IV (4)	Others	Total number
20-29	20.0	0	50.0	30.0	0	10	0	0	75.0	0	0	4
30-39	22.7	13.6	50.0	13.6	0	22	28.6	0	57.1	14.3	0	7
40-49	36.4	7.6	30.3	21.2	4.6	66	21.4	3.6	64.3	10.7	0	28
50-59	33.3	19.4	27.9	13.9	5.5	201	24.1	8.6	50.0	12.1	5.2	58
60-69	30.2	28.0	22.5	14.0	5.4	258	21.1	12.3	53.5	9.7	3.5	114
70-79	40.6	21.9	19.5	14.8	3.1	128	27.8	21.7	34.0	10.3	3.1	97
>80	27.3	22.7	31.8	9.1	9.1	22	10.4	6.9	69.0	6.9	6.9	29
	33.1	21.5	25.7	14.9	4.8	707 <sup>a</sup>	22.6	12.8	49.9	10.1	4.8	337 <sup>a</sup>

<sup>a</sup>7 male and 4 female cases with unknown age are not included.

cell types for the whole of Hong Kong and cell type specific rates are not available nor will they be very reliable because of the variation in standards and procedures of clinical and/or pathological diagnosis. However, if the proportional distribution of cell types can be accurately assessed, cell type specific rates can be calculated if the total number of cases and population data are available for the community as a whole. Opportunity for comparison is also available because there were data on 2 previous series of lung cancer cases during 2 different periods (1948-1962) (1960-1972) from the same pathology department. In the present paper, more detailed comparison is made between the 1960-1972 series and the present series (1973-1982). Comparability is maximised because we have the same source of cases and we use the same classification system. Moreover, the same exclusion criteria were adopted. Cases diagnosed with cytology and cases without histological examination of the primary tumour were excluded in both series.

The exclusion of the latter category is inevitable since malignancy cannot be confirmed and data on cell type is lacking. A bias may have however been introduced if some particular groups are not subject to any form of histological examination because of extraneous factors such as poverty and uneven distribution of medical care. The present series was derived from a pathology department which serves mainly the two most important hospitals for lung cancer on Hong Kong Island: one regional (and the only teaching hospital until 2 months ago) and one specialist chest hospital. These two hospitals are government (assisted) hospitals and the cost of hospitalisation is minimal (about £1 per day). All investigations, including pathology and treatment are free of charge. For lung cancer patients from Hong Kong Island, most of them are admitted, diagnosed and treated there, poor and rich alike. There are only a few rich patients being treated in private hospitals which only constitute a small proportion of all hospital beds in Hong Kong. Compared to the rest of Hong Kong, the proportion of lung cancer patients not being confirmed pathologically are much less on Hong Kong Island.

Apart from using the same criteria of excluding cytology cases as the previous series, another reason was because there is not yet an internationally popular classification for lung cancer cytology comparable to the one for histology by WHO. As a result a large proportion of cases is unclassified.

This is shown in the results of Lam and associates' series of 480 patients treated in the same teaching hospital as the present pathology department, which included 112 cytology cases; 35.7% (40 cases) of the cytology cases, were

unclassified. The overall unclassified proportion was also high, 13.1%. If the cytology cases were excluded, the proportion would be reduced to 6.3% which would be quite comparable with the present series.

In an earlier series by Chan *et al.* (1979), both cytology cases and cases with only radiological and clinical diagnosis were included and the unclassified proportions were even higher; 15.4% in males and 30.7% in females. This series of patients were drawn from all over Hong Kong.

Table III shows the percentage distribution in cell types in 5 series of lung cancer in Hong Kong. Both the 1976–1977 and the 1976–1980 series when compared with the 1960–1972 series shows that there is an increase in proportions of adenocarcinoma and supports the findings of the present series.

Finally, Lam *et al.* (1983) showed that survival in squamous cell carcinoma and adenocarcinoma cases was quite similar. This therefore excludes the bias due to the difference in prognosis of two types of lung cancer which may affect the proportional distribution.

With these background in mind, we compare briefly our results with those of Lee & T'so (1963) and in more detail with those of Chan & MacLennan (1977).

There are several differences between the present series and the series of Lee & T'so (1963) from 1948–1962 when lung cancer was not so common. Male predominance was not noticed until the fifth decade in their report, and the peak incidence was in the 6th decade. Adenocarcinoma was the most common histological type in both sexes, 34.8% in the male and 46.7% in the female. Although their

materials were obtained from the same department as the present series, because their case number was relatively small ( $n=228$ ) and a different classification was used, comparison and inference on time trend is not very reliable.

More reliable comparison, however, can be made with Chan and MacLennan's results (1977), because in addition to using materials from the same department with the same catchment area, they used the same classification, i.e. WHO 1967 Classification. Their case number was also larger ( $n=853$ ). We also use the same exclusion criteria as they did. There is an obvious increase in proportion of adenocarcinoma in the male from 15.6% to 25.8% ( $P<0.02$ ) and in the female from 34.3% to 49.6% ( $P<0.01$ ). The increase in adenocarcinoma is accompanied by a drop in percentage in squamous carcinoma, but not small cell carcinoma in the male. The opposite is true with the female, the increase in adenocarcinoma is associated with a decrease in small cell carcinoma but not squamous carcinoma. The proportions of large cell carcinoma remain relatively constant in both series (Table I). It is unlikely that there should be a significant inter-observer variation as the same classification is used, the sections were reviewed blind, and the changes are in squamous, small cell and adenocarcinoma which are unlikely to be confused with one another, in contrast to large cell carcinoma.

In this paper, we also compare the results obtained when different WHO classification, 1967, 1981, were used. It is useful in quantifying the change in proportional distribution of cell types when a new system is used. In Hong Kong, the new system is not commonly used yet. However, such

**Table III** Percentage distribution of histological types in 5 series of lung cancer in Hong Kong.

Series in chronological order	Males						Females					
	I	II	III	IV	Others	Total number	I	II	III	IV	Others	Total number
1. 1948–1962 <sup>a</sup> (Lee & T'so)	22.5	17.4	34.8	20.3	5.1	138	14.4	7.8	46.7	26.7	4.4	90
2. 1960–1972 <sup>a</sup> (Chan & MacLennan)	43.6	21.5	15.6	15.8	3.5	576	22.7	23.8	34.3	16.2	2.9	277
3. 1976–1977 <sup>b</sup> (Chan <i>et al.</i> )	43.3	12.5	21.6	5.3	15.4	208	23.8	9.5	33.9	2.1	30.7	189
4. 1976–1980 <sup>c</sup> (Lam <i>et al.</i> )	43.5	12.7	22.2	8.3	13.3	315	30.3	9.7	43.0	4.2	12.7	165
5. 1973–1982 <sup>a</sup> (Kung <i>et al.</i> )	33.3	21.3	25.8	14.7	4.9	714	22.6	12.6	49.6	10.0	5.3	341

<sup>a</sup>From the same pathology department serving one teaching and one chest hospital.

<sup>b</sup>From all over Hong Kong; including cytology and X Ray/clinical cases. The category of "mixed type" is not listed here.

<sup>c</sup>From the same teaching hospital as above; including cytology cases.

Note: In the 2nd to the 5th series, 1967 WHO classification was used.

quantification is useful because adjustment can be made when comparing 2 series classified on different systems especially when the new system has replaced the old one in the future.

The tendency for adenocarcinoma of the lung to increase has been noticed in three other reports (Vincent *et al.*, 1977; Cox & Yesner, 1979; Valaitis *et al.*, 1981). The increase in these studies is mainly due to increase in men. In the present report, the increase is seen in both sexes, and in fact more significantly in women.

This changing histopathological pattern of lung cancer raises again the question of the association of tobacco smoking with histological types. Although the concept that adenocarcinoma is not related to smoking has been popular since Doll *et al.* (1957) and Kreyberg (1962) published their reports, this view has been disputed by other investigators (Kennedy, 1973; Belcher, 1975). However, studies in Hong Kong and in Singapore on Chinese patients, show again that smoking is related to squamous carcinoma and small cell carcinoma but not adenocarcinoma, particularly in women (Chan *et al.*, 1979; MacLennan *et al.*, 1977). In fact, 61% of the females with adenocarcinoma did not smoke (Lam *et al.*, 1983).

The kerosene stove at one time was thought to be the cause of lung cancer in Chinese women (Leung, 1977). This association however has been shown to be weak (Chan *et al.*, 1979).

Although Schoental & Gibbard (1967) found carcinogens in Chinese incense smoke, Buddhist monks and nuns who presumably should be most heavily exposed have not been known to have a high incidence of lung cancer.

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Recently, several reports suggest that passive smoking may be a cause of lung cancer in women (Hirayama, 1981 & 1983; Trichopoulos *et al.*, 1981). This is being investigated in Hong Kong (by THL, ITMK and others).

Up to now, the cause of adenocarcinoma of the lung in non-smoking women in Hong Kong remains unknown. Investigations into environmental factors so far has been inconclusive. Although attention is mainly focussed on lung cancer in female in Hong Kong because of the high proportion of non-smokers among the patients with the predominating adenocarcinoma, it is important to realize that there is an increase of adenocarcinoma in males also over the years. Moreover, 22% of male adenocarcinoma cases were non-smokers compared to 4% and 3% in squamous and small cell carcinoma respectively (Lam *et al.*, 1983). The reason for this increase in adenocarcinoma in both males and females is at present uncertain. It is possible that the same aetiological agents operate in both men and women. Environmental and genetic factors may act synergistically. This latter argument is perhaps supported by the observation that adenocarcinoma patients in both sexes are generally younger than those with other histological types. Aryl hydrocarbon hydroxylase level in various tissues in lung cancer patients is being investigated (by ITMK and others).

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