

Lung Cancer: A review of 589 Malaysian patients

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Summary

Between 1978 and 1986, 589 patients with primary lung cancer were seen at the National Tuberculosis Centre, Kuala Lumpur. Eighty-three per cent were male and most were aged from 40 to 80 years. The patients were predominantly Chinese and 87% were current smokers or ex-smokers. The cell type was known in 538 patients (91%). There was a larger proportion of adenocarcinoma in the women than the man (42% v 25%; $p < 0.01$), in patients aged 50 years and under ($p < 0.01$) and in non-smokers than smokers (48% v 26%; $p < 0.01$). Only 27 patients (5%) underwent surgical treatment; the other patients had radiotherapy, chemotherapy or symptomatic treatment. Problems with management of patients with lung cancer in Malaysia are discussed.

Key words: Lung cancer, Malaysian patients; patient characteristics; management.

Introduction

Lung cancer has become one of the most important causes of cancer mortality in economically developed countries over the past four decades.¹ There is evidence that the incidence of lung cancer is rising in developing countries and past reports indicate that lung cancer is common,² and a leading cause of cancer mortality in Malaysia.³ Here, we present the data on a series of lung cancer patients seen at the National Tuberculosis Centre, Kuala Lumpur.

Materials and methods

A retrospective study was made from clinical records of patients in whom the diagnosis of primary lung cancer was made at the National Tuberculosis Centre (NTBC), Kuala Lumpur, during the nine year period from 1978 to 1986.

Details including age, sex, race, smoking history, symptoms, results of investigations, treatment and outcome were recorded. The diagnosis of lung cancer was made on the basis of positive histology or cytology. In the 51 patients in whom the cell type was unknown, malignant cells of unspecified cell type were identified on bronchoscopic specimens (34), percutaneous lung biopsy (2), cervical lymph node biopsy (1), sputum cytology (1) and the diagnosis in the remaining 13 patients were based on chest X-ray opacity associated with superior renocaval obstruction (9). Patients in whom detailed examination of the clinical records raised the question of secondary carcinoma were excluded from this study. Group differences were tested using the chi-square method.

Table I
Number of patients with lung cancer according to year of diagnosis

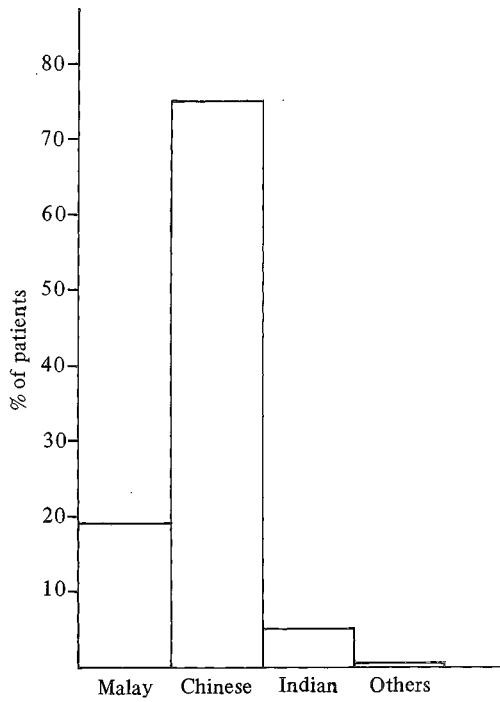
Year	Male	Female	Total
1978	7	8	15
1979	29	7	36
1980	15	3	18
1981	28	1	29
1982	22	9	31
1983	21	4	25
1984	45	13	58
1985	115	23	138
1986	206	33	239
1978 – 1986	488	101	589

Results

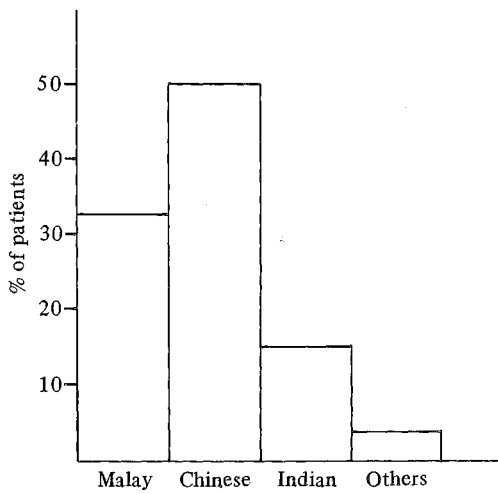
A total of 589 cases of lung cancer were studied. A rise was seen in the number of lung cancer patients from 1984 onwards (Table I). There were 488 males (83%) and 101 females (17%). At the time of diagnosis 20 patients (3%) were aged 40 years or under, 76 (13%) aged 41–50, 175 (30%) aged 51–60, 190 (32%) aged 61–70, 112 (19%) aged 71–80 and 16 (3%) were aged over 80 years. The age range was 26 to 92 years. The patients comprised 111 Malays (19%), 443 Chinese (75%), 27 Indians (5%) and 8 (1%) from other ethnic groups (Fig. 1A). The ethnic distribution of hospital attenders at the NTBC during the study period is shown in Fig. 1B. Among the major ethnic groups the Chinese accounted for a higher proportion of lung cancer cases than expected from the hospital attendance figures, with a correspondingly lower proportion of cases among the Malays and Indians ($p < 0.01$).

Smoking: The smoking history was available in 562 patients and of these, 489 (87%) were smokers. Within this group were 43 ex-smokers who had stopped smoking up to 10 years previous to the time of presentation. 94% of the males were smokers whereas only 53% of female patients had a history of smoking ($p < 0.01$).

Cell type: The cell types was identified in 538 cases (91%). Squamous cell carcinoma accounted for 55% of cases, adenocarcinoma 28%, small cell carcinoma 12%, anaplastic/large cell carcinoma 4%, and other types of carcinoma (5 cases of adenosquamous carcinoma and 1 of mucoepidermoid carcinoma) for the remaining 1%.



(A) Patients with lung cancer



(B) Hospital attenders

Fig. 1 Ethnic distribution of lung cancer patients and hospital attenders

Table II
Methods used for cell typing*

Method	No.	% patients
Bronchoscopy (biopsy and/or cytology)	351	65.2
Sputum cytology	174	32.3
Pleural fluid cytology	34	6.3
Percutaneous needle biopsy	29	5.4
Pleural biopsy	16	3.0
Lymph node biopsy	14	2.6
Thoracotomy	8	1.5
Pericardectomy and pericardial fluid cytology	1	0.2
**Liver biopsy	1	0.2

* In 17% of cases more than one investigation was positive.

**The patient had liver metastasis and was confirmed to have squamous cell carcinoma on liver biopsy but died before bronchoscopy could be done.

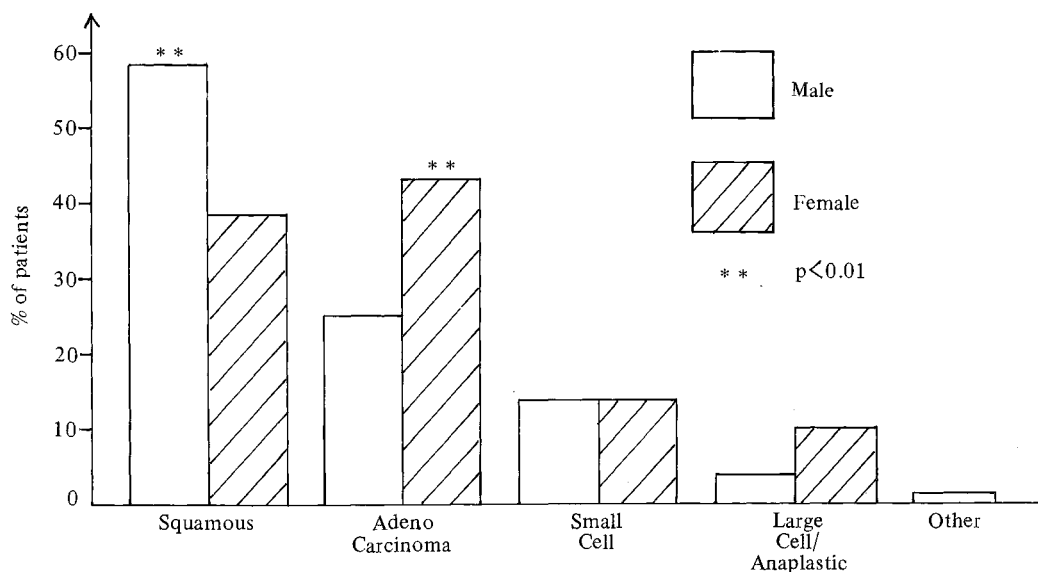


Fig II Percentage of tumours in males and female according to cell type

The methods used for determining the cell type are shown in Table II. The 93 women in whom the cell type was known had a higher proportion of adenocarcinoma (25%) and a lower proportion of squamous cell carcinoma (38% v 58%; $p < 0.01$) than the men (Fig. 2).

With respect to age, patients aged less than or equal to 50 years had significantly more adenocarcinoma (42% v 26%; $p < 0.01$) than patients aged over 50 years.

Among the major ethnic groups Malays had a smaller proportion of squamous cell carcinoma (45% v 57%; $p < 0.05$) than the other races, and Chinese had more squamous cell carcinoma (57% v 46%) and less adenocarcinoma (26% v 36%; $p < 0.05$) than non-Chinese. There were significant differences in the cell type based on smoking habit. Smokers had a larger proportion of squamous cell carcinoma (56% v 38%) and a smaller proportion of adenocarcinoma (26% v 48%; $p < 0.01$) than non-smokers. The smoker: non-smoker ratio was 9.5 : 1 and 15.5 : 1 for squamous cell and small cell carcinoma whereas it was 3.5 : 1 and 5.3 : 1 for adenocarcinoma and anaplastic/large cell carcinoma.

Association with Pulmonary tuberculosis

There were 55 patients who had had pulmonary tuberculosis in the past, up to 30 years before presentation. Twenty-four patients had concurrent pulmonary tuberculosis and in these patients sputum direct smear for AFB alone was positive in 9 cases, sputum culture for **Myobacterium Tuberculosis** was positive in 8 cases and both sputum direct smear and culture were positive in 6 cases. One patient was treated for pulmonary tuberculosis after histopathological examination of the pneumonectomy specimen showed tuberculoid granuloma adjacent to carcinoma. Another 29 bacteriologically therapeutic trial before the diagnosis of lung cancer was made. The cell types in patients with previous pulmonary tuberculosis comprised mainly squamous carcinoma (73%) and adenocarcinoma (18%), while in those with concurrent tuberculosis, these values were 77% and 18% respectively.

Table III
Clinical features of lung cancer patients at presentation

Symptoms	No.	% of patients
Cough	532	90.3
Loss of weight	401	68.1
Haemoptysis	273	46.3
Loss of appetite	233	39.6
Breathlessness	208	35.3
Chest Pain	194	32.9
Clubbing	125	21.2
Fever	81	13.8
Hoarseness of voice	42	7.1
Swelling of face/neck (SVC obstruction)	40	6.8
Dysphagia	12	2.0
Asymptomatic	1	0.2

Table IV
Radiological findings in patients in lung cancer

Radiological Feature	No.	% of patients
Mass lesion	237	40.2
Hilar Mass	213	36.2
Collapse/consolidation	133	22.6
Pleural effusion	127	21.6
Extensive bilateral infiltrates	18	3.1
Coin lesion	4	0.7
Elevated hemidiaphragm	21	3.6

Table V
Site of metastases in 166 patients with lung cancer

Site	No. (%)
Lymph nodes (Cervical 76, axillary 4)	80 (43)
Other lung	38 (21)
Bone	34 (18)
Liver	13 (7)
Brain	11 (6)
Skin	6 (3)
Pericardium	3 (2)
Total	185*

* Metastases were detectable in one site in 150 cases (90%), two sites in 13 (18%) and three sites in 3 (2%).

Clinical and Radiological features: The clinical features at presentation and radiological findings are shown in Tables III and IV. Cough was the commonest presenting complaint followed by loss of weight and haemoptysis. Only one patient was asymptomatic and 88% of patients had symptoms of less than six months' duration. Hilar masses were more common in patients with small cell carcinoma than the other cell types and pleural effusions were predominantly a feature of adenocarcinoma and large cell carcinoma rather than squamous cell or small cell carcinoma. Non-metastatic manifestations were relatively uncommon including SIADH.

At the time of diagnosis 166 patients (28%) had evidence of metastases, the most common sites being lymph nodes and contralateral lung (Table V). At initial assessment, 402 patients were found to be inoperable because of advanced disease; another 36 were inoperable because of poor general condition, advanced age or other contraindications such as poor lung function; and the disease state^{4,5} could not be determined from the available data for 199 patients, in whom there was no evidence of extrathoracic spread, but the possibility of involvement of the mediastinal lymph nodes and other central thoracic structures had not been ruled out.

Treatment and Outcome:

The initial treatment was surgery in 27 patients (5%) and of these 4 were found to be unresectable and therefore had thoracotomy only. In the other patients, radiotherapy was the initial treatment for 179 patients (30%), 17 (3%) had chemotherapy and the remaining 366 (62%) had symptomatic treatment only. The outcome was not known for 491 patients who had been lost to follow-up, 94 patients were known to have died and 4 were still on follow-up at the NTBC (including 3 who had undergone surgical resection).

Discussion

The National Tuberculosis Centre has been a referral centre for the management of patients with tuberculosis and the headquarters of the National Tuberculosis Control Programme since its inception in 1961. In recent years it has become a national referral centre for the management of other chest conditions, in particular for the diagnosis and treatment of patients with lung cancer. The main reasons are the availability of diagnostic procedures such as fiberoptic bronchoscopy and access to facilities for thoracic surgery and radiotherapy which are generally not available at peripheral hospitals.

The rise in the number of patients with lung cancer from 1984 onwards reflects to some extent the increasing number of patients with disorders other than tuberculosis seen at the NTBC: 12% (214/1734) in 1980 compared with 39% (795/2016) in 1986.

In this series, 87% of the lung cancers occurred in smokers, and most of the patients were aged 40 to 80 (94%). The aetiological association between lung cancer and cigarette smoking has been well established since the epidemiological studies of Doll and Hill^{6,7} and the lag period from the onset of smoking to malignant change is 20 to 30 years⁸ giving a peak incidence around the age of 60.

The reasons for the preponderance of Chinese patients can be speculated upon. There are no statistics on differences in smoking habits of the ethnic groups in the general population and population studies on the prevalence of smoking in the various ethnic groups would be necessary in order to determine whether a larger proportion of the Chinese smoke compared to other races. Other contributory factors may be atmospheric pollution and industrial exposure since the Chinese tend to be concentrated in urban areas.

In this group of patients 17% were female, giving a male: female ratio of 4.8 : 1. Adenocarcinoma was the most common type of lung cancer in female patients and interestingly 61% of our female patients with adenocarcinoma were non-smokers. A high incidence of adenocarcinoma of the lung occurring in non-smoking females has been reported in other countries including Hong Kong⁹ where investigations into the role of passive smoking, use of kerosene stoves and other factors have so far failed to identify the aetiological agent.¹⁰ It has been suggested that lung cancer, in particular adenocarcinoma, may arise in old tuberculous scars.¹¹ In this study, the lung cancers which occurred in patient with old pulmonary tuberculosis were mainly squamous cell carcinomas, and the association may have been coincidental since most of these patients were smokers as well (47/55).

Four percent of our patients had concurrent pulmonary tuberculosis and two-thirds of these patients had a negative tuberculin test indicating some degree of anergy. Carcinoma of the lung may reactivate tuberculosis by causing general debility and lowering resistance, or by breaking into an old tuberculosis focus. In addition, the diagnosis of lung cancer may be delayed or made more difficult by concurrent active pulmonary tuberculosis.¹² However the association may again be coincidental since both diseases are relatively common in middle-aged and elderly males.

Local customs and cultural beliefs played an important part in the management of our patients. Some patients were not willing to undergo further investigations once the diagnosis was known, and a number did not wish to have surgery, radiotherapy, or chemotherapy. This accounts for the rather low treatment rates for surgery (5%), radiotherapy (30%) and chemotherapy (3%). Survival data was difficult to obtain because many patients were referred back to their own states for follow-up at peripheral hospitals. Those treated by the Department of Oncology, General Hospital, Kuala Lumpur, were followed up there after radiotherapy and/or chemotherapy. In addition some patients (or their relatives) requested for discharge from hospital when their condition became terminal, and others did not return for follow-up of their own accord.

In general, patients with lung cancer have a very poor prognosis. Surgical resection offers the only chance of cure but this is a remote possibility because in most series 80% of patients are already unsuitable for resection at the time of diagnosis. Even after surgery only 25–30% survive for 5 years.¹³ Given this gloomy outlook and the special problems of management in Malaysian patients, more efforts should be directed towards early detection and primary prevention, in particular the prevention of cigarette smoking.

References

1. Crofton J, Douglas A. Lung Cancer. In: Respiratory Diseases (3rd ed). Oxford: Blackwell, 1981: 631–33.
2. Menon MA, Saw HS. Lung Cancer in Malaysia. *Thorax* 1979; 34 : 269–73.
3. Lim HH. Cancer mortality in the Federal Capital of Malaysia. *Sing Med J* 1986; 27 : 512–18.
4. American Thoracic Society. Clinical staging of primary lung cancer. ATS official statement. *Am Rev Respir Dis* 1983; 127 : 659–64.
5. Spiro SG. The staging of lung cancer. In: Flenley DC (ed). *Recent advances in respiratory medicine* 4. Edinburgh: Churchill Livingstone, 1986: 261–75.
6. Doll R, Hill AB. A study of the aetiology of carcinoma of the lung. *Br Med J* 1952; 2 : 1271–86.
7. Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British doctors. *Br Med J* 1976; 3 : 1525–36.

8. Geddes DM. The natural history of lung cancer: a review based on rates of tumour growth. *Br J Dis Chest* 1979; 73 : 1-17.
9. Lam WK, So SY, Yu DYC. Clinical features of bronchogenic carcinoma in Hong Kong - a review of 480 patients. *Cancer* 1983; 52 : 369-76.
10. Lam WK. The epidemiology of lung cancer in Hong Kong - a review of recent studies. *Asian Med J* 1987; 30(6) : 347-51.
11. Spencer H. Carcinoma of the lung. In: *Pathology of the Lung* (4th ed). Oxford: Pergamon, 1985 : 885-92.
12. Berroya RB, Polk JW, Raju B, Bailey AH. Concurrent pulmonary tuberculosis and primary carcinoma. *Thorax* 1971; 26 : 384-87.
13. Belcher JR. Thirty years of surgery for carcinoma of the bronchus. *Thorax* 1983; 38 : 428-32.