

Lung Cancer in Malaysia – Epidemiology and Management Practices

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Epidemiology

In Malaysia, lung cancer accounts for 13.8% of all cancers in males and 3.8% of all cancers in females.¹ The male to female ratio in terms of incidence of lung cancer is 2.8. Lung cancer is the leading cause of cancer deaths accounting for 19.8% of all medically certified deaths due to cancers.² The National Cancer Registry of Malaysia was only established in the year 2002 and there were no comprehensive statistics on lung cancer for the country before this.¹ Based on published series,^{3,4,5,6} there had been a change in the distribution of lung cancer cell types in Malaysia in recent years similar to what has been observed worldwide.⁷ While squamous cell carcinoma (SCC) was the most common cell type in the past, adenocarcinoma is the most common cell type in recent years.⁶ In the past, SCC was the most frequent cell type in men and among smokers and adenocarcinoma was the most frequent cell type in women and among never smokers.³ In recent years, adenocarcinoma was the most common cell type in both in both men women and in smokers and never smokers.⁶ The change in the distribution of lung cancer cell types in our patients over the two periods was unlikely to be due to a change in the smoking rate in our patients since the proportions of our lung cancer patients during the two periods who smoked were similar.⁶

The smoking prevalence rates in the Malaysian population based on a 1996 survey are 49.2% for male subjects and 3.5% for female subjects aged 18 years and above.⁸ Majority of male lung cancer patients are smokers. In a single institution study, the percentage of male patients with lung cancer who were ever smokers had increased significantly from 86.2% in an earlier period of 1967-1976 to 92% in 1991-1999 period while the percentage of female patients who were smokers did not change significantly between the two periods.⁶ Female patients constituted about 60-70% of patients who were never smokers with lung cancer in both periods. It has been noted by others that women are considerably over-represented in the group of non-smokers with lung cancer particularly in Asian populations.^{9,10} As described in the literature,^{11,12} the association with smoking was the strongest for our patients with small cell lung cancer (SCLC) and SCC and much less pronounced for adenocarcinoma with only slightly more than 60% of our patients with adenocarcinoma being ever smokers.^{3,6} There are, however, gender differences. While the association with smoking was true for SCLC, SCC, LCC and adenocarcinoma in our male patients; it was true only for SCLC and SCC in our female patients as the majority of our female adenocarcinoma patients were never smokers. The high incidence of female non-smokers with adenocarcinoma often seen only in the Asian population has been reported by others.⁹

The age of peak incidence of lung cancer in Malaysia is the 7th decade of life.⁶ Lung cancer is diagnosed in never smokers at a younger age (mean age, 54.7 years) than smokers (mean age, 61.6 years); and this pattern is true for both males and females.⁶ Other authors had also reported that non-smokers were diagnosed to lung cancer at a mean age which was younger than that of smokers in Asian countries like Hong Kong Singapore, Taiwan and Japan.^{9,10,13,14} This is in contrast to Western populations where smokers are more likely to have lung cancer at a younger age than non-smokers

because of the dose-response relationship between smoking exposure and lung cancer.¹⁵ In addition, our patients with adenocarcinoma tend to be younger age than those with the other lung cancer cell types. This is in agreement with other studies which show that adenocarcinoma is the predominant cell type among younger patients.^{13,16,17,18}

A high percentage of non-smoking female patients with adenocarcinoma and a younger age of diagnosis of adenocarcinoma and in non-smokers suggest that risk factors other than active smoking may be involved in carcinogenesis in these patients and in lung adenocarcinoma.

The Malaysian national cancer registry shows that the age-standardised incidence of lung cancer for the Chinese is more than twice that of the Malays and Indians for both sexes.¹ The reason for this racial difference in predisposition to lung cancer is unclear. It is possible that environmental risk factors, such as diet, may condition the risk in the Chinese, or perhaps there are racial differences in the way in which tobacco is metabolized.¹⁹

Management practices

The healthcare system in Malaysia is divided into the public sector where the majority of patients seek medical attention for specialist treatment, and the private sector where most people seek primary healthcare. Specialist treatment and hospitalisation in the public healthcare system is heavily subsidised by government funding while treatment in the private sector is paid out-of-pocket by the patients or by medical insurance.

Patients with clinical stage I or II non-small cell lung cancer (NSCLC) undergo curative surgical resection. However, three quarters of our patients with NSCLC present with stage III or IV disease and therefore curative surgery is an infrequent option.²⁰ There is significant delay in the diagnosis of lung cancer, the median patient delay being 60 days (interquartile range, 30-150 days) and the median doctor delay being 33 days (interquartile range, 18-72 days).²¹ Patient factors contributing to the delay in diagnosis of lung cancer include the failure to recognise their symptoms as serious and warrant medical attention, “shopping” for doctors and hospitals, patients’ own personal beliefs in traditional complementary medicine and patients not wanting investigations to be carried out. Among the causes of delay encountered in the healthcare system are a “loose” private sector primary healthcare system where patients hop from one primary care practice to another, low doctor:patient ratio in the public sector, delays in investigations due to long queues.

In a single institution study, only 8% of patients with NSCLC underwent surgical resection.²² Of patients who underwent surgery, 52% had SCC and 27% had adenocarcinoma and 52% had surgical-pathological stage I. Following surgery, the 5-year survival was 29% and the median survival was 27 months.

For patients with stage IIIA NSCLC and clinically evident but potentially respectable N2 disease with non-bulky mediastinal lymph node involvement and T1-3 primary tumors, a combined modality treatment approach is usually taken. Treatment options include preoperative induction therapy with chemotherapy or chemoradiotherapy; or definitive treatment with chemotherapy and radiotherapy (RT) given in a sequential fashion or concurrently. As per the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology, 2008,²³ induction chemotherapy with or without RT is

considered for patients with T1-2 N2 disease. Definitive concurrent chemoradiotherapy is also offered for this type of lesion and is the treatment for patients with T3 N2 disease. Surgical resection is considered if there has been a good response to the induction/definitive treatment. However, very few patients qualify for this latter form of treatment. In Malaysia, cytotoxic chemotherapy is prescribed by oncologists, the majority of whom are radiation oncologists and a handful of medical oncologists, and some respiratory physicians.

Patients with unresectable stage IIIB NSCLC due to T4 primary tumours, bulky N2 disease, or N3 disease, usually receive platinum-based doublet chemotherapy (gemcitabine, paclitaxel, or vinorelbine) if they have good performance status with RT being considered for palliation of local symptoms. Stage IIIB disease due to the presence of a malignant pleural or pericardial effusion is managed primarily with platinum-based doublet chemotherapy alone. Patients with stage IV disease and who have good performance status are treated with platinum-based doublet chemotherapy or single agent chemotherapy or supportive care alone for those with poor performance status. Docetaxel and more recently, pemetrexed are the standard second-line chemotherapeutic agents. With emerging evidence that non-smoking East Asian patients with adenocarcinoma have a tendency to respond to epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs) these agents are increasingly used in the second- and third-line settings, and sometimes even in the first-line setting²⁴ especially in patients with poorer performance status. However, tests for EGFR mutations, expression or gene copy numbers are rarely if ever performed. Our patients find treatment with oral medication more appealing than intravenous cytotoxic chemotherapy because of the convenience of self-administered oral therapy and also because of the perceived toxicities and side-effects associated with cytotoxic chemotherapy.

SCLC accounts for 12% of all lung cancer cases.⁶ In recent years, the incidence of SCLC seems to be on the decline. Two-thirds of cases of SCLC are diagnosed with advanced stage disease. The standard first-line chemotherapy for SCLC is platinum and etoposide doublet. Concurrent chemoradiotherapy is increasingly used for limited stage disease. Single-agent irinotecan is the standard second-line agent used.

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