

SMOKING STATUS AFFECTING SURVIVAL OF ADENOCARCINOMA LUNG CANCER PATIENTS IN KUALA LUMPUR, MALAYSIA

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ABSTRACT

Objective: Adenocarcinoma (AC) of the lung is now the most common histologic type of non-small cell lung cancer (NSCLC) worldwide since the past 20 years. This study was conducted to investigate survival difference among smoker and non-smoker lung AC patients.

Methods: A retrospective observational study was conducted for 81 advanced NSCLC adult Malaysian patients in Radiotherapy and Oncology Clinic at Hospital Kuala Lumpur, Malaysia. A total of adult 30 Malaysian smokers and 51 non-smokers with lung AC were included. Ex-smokers were not included in the study. Demographic and clinical data were collected and described. For survival analysis, Kaplan–Meier test and log-rank test were used to calculate overall survival (OS) and analyse the difference in the survival curve. Cox proportional hazard model was used to identify prognostic significance of smoking status.

Results: Non-smokers showed a significant association with female gender and Stage IV NSCLC. The median OS was higher for non-smokers (493 days) as compared to smokers (230 days). The Cox proportional hazard model showed higher hazard ratio for smokers.

Conclusion: Non-smoking is an independent positive prognostic factor in lung AC.

Keywords: Adenocarcinoma, Smokers, Survival.

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INTRODUCTION

Lung cancer is becoming one of the leading causes of cancer-related mortality worldwide [1]. The vast majority of lung cancer cases are attributed to smoking [2]. The smoking epidemic has been steadily decreased in developed countries whereas augmenting in underdeveloped and non-developed countries [3]. Non-small cell lung cancer (NSCLC) accounted for almost 80% of all lung cancer cases, comprising several histological types, including adenocarcinoma (AC), squamous cell carcinoma (SCC), and large cell carcinoma (LCC) [4]. Over the past 20 years, AC lung cancer had dramatically replaced SCC as the most frequent histologic type of 20% of lung cancer cases to approximately 40% [5]. The possible factor among smokers being the most frequent histologic type NSCLC included changes in the smoking trend from high-tar to low-tar filtered cigarettes [6]. Low-tar filtered cigarette result in deep and intense inhalation of tobacco smoke leading to greater delivery of carcinogens such as nitrogen oxide and nitro salted compounds to the lung periphery [7]. Passive smoking contributed to the shift in the cell type of NSCLC among non-smokers as a result of rapid inhalation of gaseous components of cigarette smoke into the deeper parts of the lungs as compared to the mainstream smoke containing more particulates [8].

This study was conducted to glance for the survival differences among smokers and non-smokers in lung AC. Since the mechanism of carcinogenesis of AC arising in smokers and non-smokers is distinct, it would imply differences in demographic and clinical characteristics and hence survival.

METHODS

This was a retrospective review of patients with NSCLC diagnosed at Radiotherapy and Oncology Clinic, Hospital Kuala Lumpur, Malaysia,

from January 2009 to December 2012. The study was approved for research ethics by Medical Research and Ethics Committee, Ministry of Health, Malaysia. Patients' ≥ 18 years old histopathologically confirmed to have locally advanced or metastatic AC were included in the analysis. Retrospectively collected demographic and clinical variables included gender, age (at diagnosis), stage of NSCLC, and smoking status. Data regarding smoking status included current smokers and non-smokers whereas ex-smokers were not included in the study. For survival analysis, each patient's time began on the date of diagnosis of disease and ended on the date of last follow-up for living patients and date of death for dead patients. Survival time was calculated in days. Furthermore, cancer-specific mortality was documented. Deaths resulting from any non-cancer causes were excluded from the study.

Statistical analysis was performed using SPSS 21.0 version. Demographic and clinical data were analysed descriptively by dividing the study population into two cohorts; smokers and non-smokers. Pearson χ^2 tests were used to compare demographic and clinical variables among groups based on smoking status. The primary end point of this study was overall survival (OS). Survival was calculated using Kaplan–Meier test and compared using log-rank test. Prognostic importance of smoking status in lung AC was analysed using Cox proportional hazard model. A two-sided $p < 0.001$, $p < 0.05$ were considered statistically significant.

RESULTS

Characteristics of study Malaysian population categorised as smokers and non-smokers are listed in Table 1. There were 30 smokers and 51 non-smokers out of total 81 NSCLC AC patients (37.0% and 63.0%, respectively). There were more male smokers (32.0%) than male non-smokers (18.5%). Most patients in both groups were between

Table 1: Demographic and medical variables of patients

Characteristics	Smoker's n (%)	Non-smoker's n (%)
Total patients (n=81)	30 (37.0)	51 (63.0)
Gender		
Male	26 (32.0)	15 (18.5)
Female	4 (5.0)	36 (44.4)
Age (years old)		
18-40	2 (2.4)	5 (6.1)
41-64	24 (29.6)	38 (47.0)
≥65	4 (5.0)	8 (10.0)
NSCLC stage		
III A	4 (5.0)	2 (2.4)
III B	9 (11.1)	6 (7.4)
IV	17 (21.0)	43 (53.0)

NSCLC: Non-small cell lung cancer

Table 2: Overall survival of smokers versus non-smokers

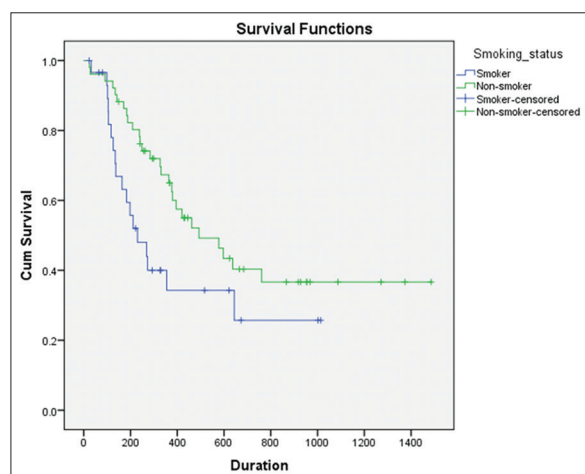
Smoking status	Median OS (days)	95% CI	p
Smoker	230	115.092-344.908	0.039*
Non-smoker	493	262.284-723.716	

OS: Overall survival, CI: Confidence interval, *p<0.05

Table 3: Survival analysis by Cox proportional hazard model

Parameter	HR (95% CI)	p
Male versus female gender	0.914 (0.509-1.643)	0.764
Smoker versus non-smoker	1.865 (1.022-3.406)	0.042*
Increasing age	0.836 (0.433-1.614)	0.593

HR: Hazard ratio, CI: Confidence interval, *p<0.05

**Fig. 1: Kaplan-Meier overall survival curve for smoker versus non-smoker**

41 and 64 years old (29.6% smokers vs. 47.0% non-smokers) and having Stage IV NSCLC (21.0% smoker vs. 53.0% non-smokers). There

were statistically significantly higher percentages of female ($p<0.001$) and Stage IV NSCLC ($p=0.022$) patients in the non-smokers category. Median OS was 230 days for smokers and 493 days for non-smokers ($p=0.039$) (Table 2). Kaplan-Meier survival curve for smokers versus non-smokers is shown in Fig. 1. The hazard ratio (HR) for smokers was 1.865 times higher as compared to non-smokers ($p=0.042$) (Table 3).

DISCUSSION

It is presumed that carcinogenic and mutagenic chemicals in the cigarette smoke induce lung carcinogenesis in smokers. However, non-smokers dictate distinct natural history and mechanism of carcinogenesis. The analysis was performed to determine disparities in patient characteristics and their survival among smokers and non-smokers with lung AC.

The results of this study showed that females having lung AC were more likely to be non-smokers as compared to males. A similar result was also reported by a West Japan Oncology Group study that lung AC patients were mostly to be female non-smokers [9]. The statistically higher percentage of Stage IV NSCLC in non-smokers might be because this study comprised a higher proportion of Stage IV (74.0%) and non-smoker (63.0%) AC patients. OS was longer, and HR to death was less for non-smokers as compared to smokers. Similarly, a prospective study reported that non-smoker lung AC patients had improved OS and non-smoking showed positive prognostic significance in lung AC [10].

CONCLUSION

In conclusion, this study demonstrated that smoking status has a prognostic impact in patients with lung AC.

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