INTRODUCTION
Non-small cell lung cancer (NSCLC) is one of the growing public health problems in Malaysia. At diagnosis, most patients presented with inoperable advanced disease [1]. Locally advanced or metastatic disease treatment is palliative not curative. In advanced NSCLC, prognosis is the fundamental factor that influences the treatment decisions. Better prognostic tools are needed to avoid the use of unnecessary, harmful therapy in the end-stage life. Lung cancer treatment guidelines advise performance status (PS) as the most established factor for assessing prognosis [2].

PS is the assessment of patient’s fitness. It measures the impact of tumour symptoms, together with other pre-existing medical problems with a patient’s daily life and ability of self-care [3]. In oncologic practice, PS is widely used as it correlates with survival duration of patients [4]. Two most commonly employed scales are the Karnofsky scale [5] created at the beginning of chemotherapy era and the Eastern Cooperative Oncology Group scale (ECOG) of PS. ECOG PS is an evaluation scale of 0-5 based on the level of symptoms affecting normal activity and the proportion of waking hours spent in bed [6]. ECOG PS scores are described in Fig. 1. PS is a strong independent prognostic factor of survival in advanced NSCLC [7,8].

Numerous studies are available on the prognostic significance of PS in advanced NSCLC patients mainly from developed countries. However, to date, no such data are published in Kuala Lumpur, Malaysia. Therefore, the present study aimed to investigate the prognostic significance of PS in advanced NSCLC adult Malaysian patients. Data obtained from this study later may help the clinical oncologists and clinical pharmacists, especially in Kuala Lumpur, Malaysia, to use ECOG PS as a more effective prognostic tool in advanced NSCLC adult Malaysian patients.

METHODS
A retrospective observational study was conducted at Radiotherapy and Oncology Clinic, Hospital Kuala Lumpur, Malaysia, between 1 September 2014 and 31 January 2015. The study was approved by Postgraduate Academics and Ethics Committee, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Research Ethics Committee, Research Management Institute and Medical Research and Ethics Committee, Ministry of Health, Malaysia.

This study included 163 adult Malaysian patients (≥18 years old) that had histological confirmed locally advanced (Stage III A) or metastatic (Stage III B, Stage IV) NSCLC and was on chemotherapy treatment. Age, gender, body weight, clinical stage, and ECOG PS score were noted at the time of diagnosis of disease. To calculate survival time, date of diagnosis, date of the last follow-up and date of death were recorded.

Statistical analysis was conducted using SPSS 21.0 version. Demographic and medical data variables were analyzed descriptively. Pearson χ² tests were used to find the association of demographic and medical data variables with categories of ECOG PS. Multinomial logistic regression was carried out to find the relationship of ECOG PS with patient’s demographic and medical data. For survival analysis, survival time was calculated in days and defined as the time from diagnosis of the disease until death or censored if alive or lost follow-up. To evaluate the prognostic significance of PS, Kaplan-Meier method was used to measure median overall survival (OS) time for ECOG PS scores and
RESULTS

There were 163 patients included in the study. The overall mean age of enrolled patients was 56.7±10.1 years old. Most were male, having overall mean body weight 57.42±13.5 kg and Stage IV NSCLC (Table 1). ECOG PS showed significant association with age and body weight (Table 2). There was no significant relationship between ECOG PS and other independent study variables. Majority patients had an ECOG PS of 2 (41.1%) followed by 35.0% having ECOG PS of 3. Univariate overall survival analysis for EOG PS scores of advanced NSCLC patients showed that median OS for PS=2 was 377 days, for PS=3 was 297 days, and for PS=4 was 253 days (Table 3). The difference in OS was statistically significant (p=0.003) (Fig. 2). Multivariate analysis showed that PS was the predictor of survival in advanced NSCLC patients (p<0.001) (Table 3).

DISCUSSION

In the present study, the overall mean age of the study patients at presentation was found to be 56.7±10.1 years old. The results obtained in two other published Malaysian studies by Liem et al. [9], and Hashim et al. [10] stated that overall mean age was 60.3±11.6 years old. The differences in the mean age of patients in the present study and previously published two studies might be attributed to differences in the inclusion-exclusion criteria of study. The present study only involved unresectable NSCLC patients while both previously published studies included unresectable NSCLC patients along with minor percentages of resectable NSCLC patients.

Male gender formed the predominant group of adults NSCLC patients (68.7%). Similar results were obtained in different study locations of Malaysia by Liem et al. [9], and Hashim et al. [10], where the male was more frequently suffering from NSCLC. Youlden et al. [11] stated that despite geographical differences, lung cancer had higher incidence worldwide among males as compared to females.

The current study showed that at diagnosis, most patients were suffering from Stage IV NSCLC. This finding is in agreement with a study carried out in Thailand by Kitiporn et al. [12] where Stage IV was the most common clinical stage of NSCLC. Increased frequency of metastatic NSCLC may be attributed to the late presentation and heterogeneous nature of the disease.

The results of Table 2 depicted that ECOG PS was significantly associated with age and body weight of adult NSCLC patients. Similarly, Kawaguchi et al. [13] in their study on NSCLC patients found a significant association of ECOG PS with advanced NSCLC patient demographic and medical data.

Table 1: Patient demographic and medical data

| Variable | Category | Advanced NSCLC (n=163) | n (%) |
|----------|----------|------------------------|-------|
| Age (Years old) | Mean±SD | 56.7±10.1 | 22 |
| Gender | Male | 112 (68.7) | 81 |
| Body weight (kg) | Mean±SD | 57.42±13.5 | 30 |
| NSCLC Stage | III A | 18 (11.0) | 114 |
| | III B | 39 (23.9) | 39 (23.3) |
| | IV | 106 (65.0) | 397 |

SD: Standard deviation, NSCLC: Non-small cell lung cancer

Table 2: Association of EOGO PS with advanced NSCLC patient demographic and medical data

| Variable | EOGO PS scores (n=163), n (%) | p* |
|----------|-------------------------------|----|
| Age (Years old) | 0 | 1 | 2 | 3 | 4 |
| 18-40 | 5 (3.0) | 4 (2.4) | 3 (1.8) | 1 (0.6) | 0.008* |
| 41-64 | 22 (13.4) | 40 (24.5) | 47 (28.8) | 6 (3.6) | 0.556 |
| >65 | 2 (1.2) | 23 (14.1) | 7 (4.2) | 0 (0.0) | 0.001** |
| Gender | Male | 18 (11.0) | 45 (27.6) | 40 (24.5) | 6 (3.6) |
| Female | 11 (6.7) | 22 (13.4) | 17 (10.4) | 1 (0.6) | 0.367 |
| Body weight (kg) | 30-60 | 19 (11.6) | 42 (25.7) | 39 (23.9) | 3 (1.8) |
| 61-90 | 7 (4.2) | 25 (15.3) | 18 (11.0) | 4 (2.4) | 0.001** |
| >91 | 3 (1.8) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0.367 |
| NSCLC Stage | III A | 7 (4.2) | 4 (2.4) | 6 (3.6) | 0 (0.0) |
| III B | 4 (2.4) | 21 (12.8) | 13 (7.9) | 0 (0.0) | 0.631 |
| IV | 18 (11.0) | 42 (25.7) | 38 (23.3) | 7 (4.2) | 0.367 |

*Chi-square test, *p<0.01, **p<0.05, NSCLC: Non-small cell lung cancer, ECOG: Eastern Cooperative Oncology Group, PS: Performance status

Table 3: Impact of PS on survival in advanced NSCLC patients

| Variable | n (%) | Univariate | Multivariate | p* | HR (95% CI) | p* |
|----------|-------|------------|--------------|----|-------------|---|
| EOGO PS | 0 | 3 (1.8) | - | 0.003* | 5.101 (3.291-7.907) | 0.002* |
| | 1 | 29 (17.8) | - | 0.297 (0.057-1.542) | 0.001** |
| | 2 | 67 (41.1) | 377 | 0.320 (0.157-0.655) | 0.149 |
| | 3 | 57 (35.0) | 397 | 0.617 (0.348-1.091) | 0.092* |
| | 4* | 7 (4.3) | 253 | 1.117 (0.712-1.753) | 0.902* |

*Reference group in multivariate analysis, Kaplan-Meier method, Cox proportional hazard regression, *p<0.01, **p<0.001, ECOG: Eastern Cooperative Oncology Group, PS: Performance status, OS: Overall survival, HR: Hazard ratio, CI: Confidence interval
of ECOG PS with age. Patients on diagnosis having body weight <61 kg were more frequently having ECOG PS score of 2 (25.7%) followed by ECOG PS score of 3 (23.9%). Dewys et al. [14] stated that poor body weight was associated with decreased PS. The present study demonstrated that patients with ECOG PS score of 4 had worse survival which was similar to the study by Simmons et al. [8] who also observed least survival among patients having ECOG PS score of 4. The findings of the Cox proportional hazard model suggested that hazard to death was decreased in patients with ECOG PS 0 and increased in patients with ECOG PS 2. Likewise, Radzikowska et al. [15] also found that survival was worse in ECOG PS 2 patients as compared to patients with ECOG PS score of 0. Hence, both current and later study confirmed PS as a significant independent prognostic factor for survival in advanced NSCLC.

**CONCLUSION**

PS is a strong prognostic factor of survival in advanced NSCLC. In translating this to clinical care, PS should be examined in the setting of treatment stratification among advanced NSCLC patients.

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