Survival at one year in patients with lung cancer in a tertiary care center

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Abstract

Introduction: Lung cancer is a leading cause of mortality worldwide and despite advances in treatment, prognosis of advanced lung cancer is extremely poor, with a median survival time of approximately 1year. Factors like age, sex, performance status at the time of diagnosis, histological type, extent of disease, smoking status were found to predict survival in lung cancer. **Aim of the study:** To determine one year survival of lung cancer patients from the date of diagnosis and to evaluate factors that are associated with survival. **Methodology:** Prospective cohort study, conducted at Medical College, Thiruvananthapuram, Kerala, in 160 consecutive patients with histopathological diagnosis of lung cancer. Data on demography, symptoms, smoking status, performance status according to WHO performance scale, histological diagnosis, TNM stage and death were recorded using a structured questionnaire. Proportion of patients who survived at one year from the date of diagnosis was determined. For inferential statistics between groups, comparison of qualitative variables were analysed by chi-square test and quantitative variables were compared by student t test. P value of less than 0.05 was considered as level of significance Cox proportional hazard model were used to evaluate the factors affecting survival of lung cancer patients. **Results:** 160 consecutive lung cancer patients with histopathological diagnosis were included in the study. 86.9% of patients were males. Male to Female ratio is 6.6: 1. 84. 5% of patients were above the age of 50 years. 11.3% were nonsmokers. COPD was the commonest comorbidity (58%) in the study. Adenocarcinoma (41.9%) was the commonest histological type in our study and this was the commonest histological type seen in females and nonsmokers. In smokers, squamous cell carcinoma (91.3%) was more common. 66.9% of patients were at TNM stage 3 or 4 at the time of diagnosis. 17.5% patients survived at one year after diagnosis. Age more than 70 years, high smoking index, associated COPD, TNM Stage 3 & 4, poor performance status at the time of diagnosis were associated with poor survival. (p value <0.001). Squamous cell carcinoma had better survival compared to other histological types (p< 0.001). No significant association between gender and survival pattern was seen in the study. **Conclusion:** We found that 17.5% of lung cancer patients survived at one year after diagnosis. There was significant association of factors like age, smoking status, comorbidities, histological type, TNM stage and performance status at diagnosis with survival pattern. But no significant association between gender and survival was found in our study.

Keywords: Lung Cancer, Survival, Performance status (PS), Small cell cancer (SCC), Nonsmall lung cancer (NSCLC)
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Introduction

Lung cancer is one of the commonest cause of cancer related deaths all over the world. It accounts for 13% of the total number of new cases of all cancers and 19 per cent of cancer related deaths worldwide [1]. There were 1.8 million new lung cancer cases estimated to occur in

2012. In India, lung cancer constitutes 6.9 per cent of all new cancer cases and 9.3 per cent of all cancer related deaths in both sexes, with the highest reported incidences from Mizoram [2]. The time trends of lung cancer show a significant rise in Delhi, Chennai and Bengaluru in both sexes [2]. The incidence and pattern of lung cancer differ as per geographic region and ethnicity and largely reflect the prevalence and pattern

of smoking. The overall 5-year survival rate of lung cancer is dismal with approximately 15 per cent in developed countries and 5 per cent in developing countries [3]. In Kerala scenario, 20.1% of all male cancers are due to Lung cancer [4].

In the Western countries and most of the Asian countries adenocarcinoma has surpassed squamous cell carcinoma [5,6]. This shift might be attributable partly to the smoking habits, particularly filtered cigarettes; moreover, there is also increasing incidence of lung cancer in females and non smokers [5,7,8] Studies showed that men who had never smoked, had higher age-standardized lung cancer death rates than women [7]. Lung cancer in never smokers is an important public health issue, and further exploration of its incidence patterns, etiology, and biology is needed [8]. Most of the previous Indian studies have described squamous cell carcinoma as the commonest histology [9,10] however, some recent studies from two major centers are showing a changing pattern in India [11,12].

No weight loss at the time of diagnosis was a significant predictor for long survival in addition to younger age, limited stage, good functional performance and surgical treatment [13]. The majority of mortalities occurred in elderly patients. The median survival time of elderly patients was significantly lower compared with that of younger patients [14]. The 1-year survival rates in younger and elderly patients were 67.3 and 42.5%, respectively [14]. In multivariate analysis, elderly patients also had significantly poorer survival. In the group of elderly patients, analyses revealed that significant prognostic factors, including stage of disease and serum lactate dehydrogenase (LDH) levels, were associated with survival [14] .The stage at diagnosis was a critical factor that affected the survival of lung cancer patients. So it is essential to develop early diagnosis of lung cancer [15]. The most common comorbid conditions reported are chronic pulmonary disease (52.5%), diabetes (15.7%), and congestive heart failure (12.9%). The adjusted overall survival of lung cancer patients was negatively associated with the existence of different comorbid conditions such as congestive heart failure, diabetes with complications, moderate or severe liver disease, dementia, renal disease, and COPD, depending on the stage [16]. The presence of comorbid conditions were associated with worse survival and different comorbid conditions were associated with worse outcomes at different stages [16]. There is poor prognosis across histologic subtypes in stage IV NSCLC patients. More research using other

sources of population-based data could help to clarify the role of histology in the presentation, management, and prognosis of late-stage NSCLC [17]. Current smoking at diagnosis is an important independent predictor of shortened lung cancer survival. This effect is not explained by sociodemographic/exposure factors, adverse symptoms, histology, stage, comorbidity, and treatment suggests that it may be mediated through direct biological effects [18]. Nonsmokers have a 20 to 30 percent greater chance of developing lung cancer if they are exposed to secondhand smoke at home or work. Men who smoke are 23 times more likely to develop lung cancer. Nonsmokers have a 20 to 30 percent greater chance of developing lung cancer if they are exposed to secondhand smoke at home or work [19]. Aim of this study was to determine one year survival of lung cancer patients, from the date of diagnosis and to evaluate the factors affecting survival in patients attending a tertiary care center. These factors associated with survival may be used to develop prediction models in newly detected lung cancer.

Methodology

Aim of study. To determine one year survival of lung cancer patients from the date of diagnosis and to evaluate factors that are associated with survival. **Study Design**. A prospective cohort study over a period of two years.

Study Setting: Department of Pulmonary Medicine and Department of Oncology, Medical College, Thiruvananthapuram. **Study population:** 160 consecutive patients with histopathological diagnosis as lung cancer, diagnosed at Pulmonary Medicine department or cases of lung cancers referred from elsewhere to Department Oncology, Medical College, Thiruvananthapuram, Kerala for a period of two years. **Inclusion criteria:** All cases of lung cancer with histological proof, willing to participate in the study were included. **Exclusion criteria:** Patients with malignancies other than lung cancer were excluded. **Data collection:** Information on demography, symptomatology, histopathological type of lung cancer, extent of disease according TNM classification, performance status of patients at the time of diagnosis by WHO performance scale, smoking status, co-morbidities, treatment details, address and phone numbers were collected by patient interview and medical records using structured questionnaire, after getting written consent from patients. Further follow up was done in every 3 months overphone or from

oncology department records. Data about health status of patients or date of death were recorded in every 3 months. Institutional ethical committee clearance was obtained before collecting data.

Statistical analysis: Data were entered in Microsoft Excel and analyzed using SPSS 10 version.

For inferential statistics between groups, comparison of qualitative variables were analysed by chi-square test and quantitative variables were compared by student t test.

P value of less than 0.05 was considered as level of significance

Results

160 consecutive lung cancer patients with histopathological diagnosis were included in the study. 139 (86.9%) were males and 29 (13.1%) were females.Male to Female ratio is 6.6 : 1. 84.5% of patients were above the age of 50 years and 2.5% were below 40 years .11.3% were nonsmokers.80.6% of smokers were having smoking index >200. Hemoptysis was present in 38% of patients.COPD was the commonest comorbidity (58%), followed by anemia (50%). Commonest histological type was Adenocarcinoma (41.9%). Adenocarcinoma was the commonest histological type seen in females and nonsmokers. In smokers, squamous cell carcinoma was the commonest histological type (91.3%) found, in the study. Small cell cancer (SCC) occurred in16.3%of patients.66.9% NSCLC of patients were at TNM stage 3 or 4 at the time of diagnosis whereas an 80.3% of SCC were at extensive stage. Only 5% of patients underwent surgery. 17.5% patients survived at one year after diagnosis.

Table-1: Survival function of age

Age (in years)	Survival				Total
	< 3 months	3 - 6 months	6 - 12 months	> 1 year	
30 - 39	4	-	-	-	4
	6.60%				2.50%
40 - 49	-	4	7	10	21
		11.80%	18.90%	35.70%	13.10%
50 - 59	18	15	13	16	62
	29.50%	44.10%	35.10%	57.10%	38.80%
60 - 69	17	5	6	2	30
	27.90%	14.70%	16.20%	7.10%	18.80%
>= 70	22	10	11	-	43
	36.10%	29.40%	29.70%		26.90%

Chi square: 45.321; p <0.001

Age more than 70 years was found to be associated with poor survival. (p< 0.001).

Table-2: Survival function of smoking.

History of smoking	Survival				Total
	< 3 months	3 - 6 months	6 - 12 months	> 1 year	
Non smoker	3	3	6	6	18
	4.90%	8.80%	16.20%	21.40%	11.30%
50 - 200	7	-	2	4	13
	11.50%		5.40%	14.30%	8.10%
200 - 500	6	4	6	5	21
	9.80%	11.80%	16.20%	17.90%	13.10%
500 - 1000	29	19	7	10	65
	47.50%	55.90%	18.90%	35.70%	40.60%
> 1000	16	8	16	3	43
	26.20%	23.50%	43.20%	10.70%	26.90%

Chi square: 25.974; p <0.05

High smoking index was an independent predictor of survival in the study. (p< 0.001).

Table-3: survival function of histology.

Histology	Survival				Total
	< 3 months	3 - 6 months	6 - 12 months	> 1 year	
Squamous cell carcinoma	8	6	12	20	46
	13.10%	17.60%	32.40%	71.40%	28.80%
Adino carcinoma	26	15	20	6	67
	42.60%	44.10%	54.10%	21.40%	41.90%
Small cell carcinoma	16	6	2	2	26
	26.20%	17.60%	5.40%	7.10%	16.30%
Large cell carcinoma	4	-	-	-	4
	6.60%				2.50%
Non-specific	7	7	3	-	17
	11.50%	20.60%	8.10%		10.60%

Chi square: 49.505; p <0.001

Squamous cell carcinoma had a better survival compared to other histological type. (p< 0.001).

Table-4 Survival pattern in relation to TNM staging.

| TNM(NSCLC)	Survival				Total
	< 3 months	3 - 6 months	6 - 12 months	> 1 year	
Stage I	-	-	-	3	3
				10.70%	1.90%
Stage II	-	-	-	22	22
				78.60%	13.80%
Stage IIIa	-	4	11	-	15
		11.80%	29.70%		9.40%
Stage IIIb	5	5	11	-	21
	8.20%	14.70%	29.70%		13.10%
Stage IV	31	16	2	-	49
	50.80%	47.10%	5.40%		30.60%
Limited stage (SCC)	-	-	3	2	5
			8.10%	7.10%	3.10%
Extensive stage(SCC)	16	6	-	-	22
	26.20%	17.60%			13.80%
Stage unkonwn	9	3	10	1	23
	14.80%	8.80%	27.00%	3.60%	14.40%

Chi square: 213.488; p <0.001

TNM Stage 3 & 4, at presentation was an independent factor that predict poor survival in lung cancer in our study (p< 0.002). Extensive stage of SCC predict poor prognosis.

WHO Performance score 2, 3 & 4 at the time of diagnosis were associated with poor survival. (p <0.001)
Associated comorbidities like COPD, was predictor of poor survival in our study. (p< 0.001)

No significant association between gender and survival pattern was seen in the study.
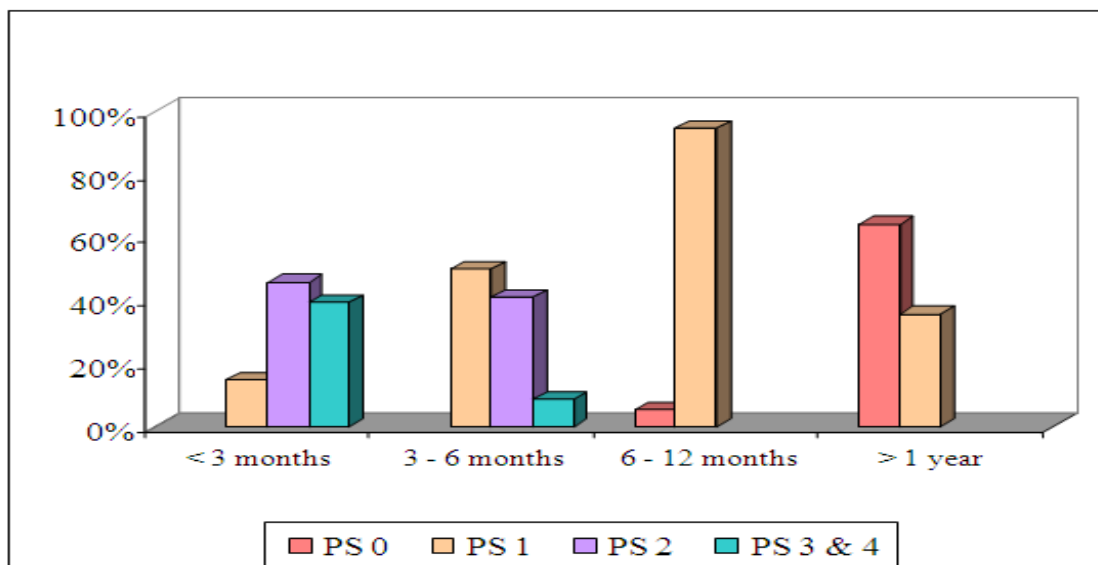
Fig-1: survival pattern in relation to performance status (WHO performance score)

Discussion

The five-year survival rate for lung cancer is 55 percent for cases detected when the disease is still localized (within the lungs). However, only 16 percent of lung cancer cases are diagnosed at an early stage. For extensive stage disease the five-year survival rate is only 4 percent. The lung cancer five-year survival rate (17.7 percent) is lower than many other leading cancer sites [19]. More than half of people with lung cancer die within one year of being diagnosed [19]. Exposure to second hand smoke causes approximately 7,330 lung cancer deaths among nonsmokers every year [19]. Previous studies carried out to find out survival pattern and factors predicting survival showed conflicting results [14,20].

Our study showed a male to female ratio of 6.6 : 1 and age group commonly affected was 50 – 59 years, findings correlating with results of other Indian study [4]. According to study by Malik PS et al median age of lung cancer patients was 55 years with a male:female ratio of 4.6:1.[12].

11.3% were nonsmokers in our study. Previous studies also reported the increasing incidence of lung cancer in females and non smokers [7,8].

Adenocarcinoma was the most common histological type encountered in our study (41.9%), a result similar to Indian study [4], but KilHoi Lee et al reported squamous cell carcinoma (39.7%) as the most frequent histological type, followed by adenocarcinoma 25.5%

[15]. In the Western countries and most of the Asian countries adenocarcinoma has surpassed squamous cell carcinoma [5,6]. This shift might be attributable partly to the smoking habits, particularly filtered cigarettes. Recent studies from two major centres are showing a changing pattern in India also.[11,12].

COPD (58%) was the commonest comorbidity in our study. Similar finding was reported by Islam K M et al, where prevalence of COPD in lung cancer was 52.5% [16].

66.9% of patients with NSCLC were at TNM stage3 or 4 at the time of diagnosis and among SCC 80.3% had extensive disease in this study as reported earlier [4].

Malik PS et al reported that 56.8% cases were of stage IV while among SCLC 71.8% cases had extensive stage disease [12].

17.5% patients survived at one year after diagnosis in our study, similar to the result in earlier study by P.A. Mahesh et al [6]. Malik PS et al reported that the median overall and progression free survivals of the patients who received treatment were 12.8 months [12].

Age more than 70 years at diagnosis was associated with poor survival in our study similar to the result of study by FarukTas et al.where median survival time of elderly patients was significantly lower compared with that of younger patient [14].

Lung cancer patients with COPD had higher mortality in the study.Studies by Islam KM et al and C.Martin et al also showed similar results [16,18,20]. Performance status 2,3 & 4 (according to WHO Performance scale) at the time of diagnosis were found to be associated with poor survival in our study. Earlier studies also demonstrated that poor performance status at diagnosis was associated with decreased survival time [13]. High smoking index was found to be an independent predictor of survival in the study. Study by Seung Jun Lee, et al reported an overall mortality of ever-smokers was higher than that of never-smokers in patients with newly diagnosed NSCLC, and current smoking was an independent risk factor for a poorer prognosis [18,21].

Squamous cell carcinoma was found to have better prognosis compared to other histological types in our study as reported earlier by Karynsa Cetin et al [17]. TNM stage was independent prognostic factor that predicted survival in this study. Kil Hoi Lee,et al also reported that stage of lung cancer was an independent factor associated with survival [15]. Our results showed no significant association between survival pattern and gender,butKil Hoi Lee et alreported that survival rate in females was higher than that of males [15].

Conclusion.

17.5% of lung cancer patients survived at one year after diagnosis. There was significant association of factors like age, smoking status, comorbidities, histological type, TNM stage and performance status at diagnosis with survival pattern, a finding that may help in developing prediction model for prognostication of lung cancer at the time of diagnosis.

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