Clinicopathological and Survival Pattern in Lung Cancer Patients of Different Age Group

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Abstract: Lung cancer is considered as disease of older population with median age of 70 year at diagnosis. The aim of this study was to investigate the clinicopathological and survival pattern in younger and older age lung cancer patients. A retrospective study was carried out for all histopathologically or cytologically confirmed cases of primary lung cancer treated between 2011 and 2015at the Regional Cancer Centre, Imphal, Manipur, India. Cases were grouped into two age groups, i.e. the younger age group (<60 year) and the older age group (≥60 year).Out of the total 432cases of primary lung cancer, 124 were diagnosed at <60year of age with median age of 55 year and 308 patients were diagnosed at ≥60year of age with median age of 70year at diagnosis. Younger age group was found to have significantly lesser number of chronic smokers (p=0.000), lesser history of pulmonary tuberculosis (p=0.019), higher rate of adenocarcinoma (p=0.000), more positive family history (p=0.008), more advanced stage (III & IV) at presentation (p=0.000), greater proportion of patients undergone combined modality of treatment and lesser proportions of patients refused active cancer treatment (p=0.002) as compared to older age group. Response to treatment in terms of median survival (p=0.338) and three year overall survival (p=0.344) was found similar in both the age groups in spite of more advanced stage of the disease at presentation in younger age group, the reasons could be lesser proportion of older age patients got combined modality treatment due to greater comorbidities, poor performance status & greater proportion of older age patients refused active cancer treatment, because of lesser expectation in terms of long term benefit with treatment.

Keywords: Age Variation, Clinicopathology, Lung Cancer, Survival

1. Introduction

Lung cancer is the most common cause of cancer-related death in the United States and worldwide [1, 2]. Despite recent advances in treatment, prognosis of patients with lung cancer remains poor, with 5-year overall survival of approximately 15%. Lung cancer is often considered a disease of the older population with a median age at diagnosis of about 70 year [3]. Some studies have suggested that younger patients with lung cancer have a more aggressive disease course and a worse prognosis than older patients [4-7], other investigators have reported that the survival of lung cancer in younger and older patient cohorts is similar [8-11], whereas some other studies have shown improved survival in younger patients [12-17]. The present study is aimed to identify and evaluate the known clinicopathological factors and to elucidate the clinical significance of patient age on the outcome of lung cancer.

2. Material and Methods

The retrospective study was carried out obtaining data from registry of Regional Cancer Centre, Regional Institute of Medical Science, Imphal, Manipur. Study population included all histopathologically or cytologically confirmed cases of primary lung cancer registered and treated between 2011 to 2015. IBM SPSS-21 version for windows was used for all data analysis. Variables like age, sex, smoking habit, family history, history of Pulmonary tuberculosis/Asthma/COPD, histopathologic subtype, stage were analyzed using Chi square analysis (two sided). P value < 0.05 was considered as

significant difference. Survival was analyzed using Kaplan Meier survival analysis and compared by log rank testing.

3. Results

3.1. Demographic Characteristics

Out of the total 432 lung cancer patients, 124 (28.7%) were <60 years and 308 (71.3%) were ≥60 years at diagnosis. Within the younger age group, 102 (82.3%) were between 50 to 59 years, 17 (13.7%) were between 40 to 49 years, and only 5 (4.0%) were between 30 to 39 years of age. The median ages of the younger and older age groups were 55 and 70 years, respectively (Table 1). The differences in distribution of disease with gender between the two age groups were not found statistically significant (p=0.451) (Table 1). History of chronic smoking was found in 61

(49.2%) patients of younger age group and 250 (81.2%) patients of the older age group, which shows a statistically significant (p=0.00) decreasing trend of smoking habit in younger age group (Table 1). This decreasing trend of smoking habit in younger patients is an indicator of successful Anti tobacco awareness programme in North Eastern India. Positive history of co morbidities like asthma or COPD was found lesser in younger age group (1.6%) compared to older age group (4.9%), though the difference was not significant (p=0.115). Positive family history of lung cancer was found significantly higher (p=0.008) among younger age group i.e. 4.8% as compared to 0.6% in older age group. Previous history of tuberculosis was found significantly lesser (p=0.01) in younger age group (7.3%)as compared to in older age group (17.5%) (Table 1).

Table 1. Demographic Characteristic.

	Age <60 (in years)N=124	Age≥60(in years) N=308	P value
Median age	55	70	
Male	69(55.7%)	184 (59.7%)	0.434
Female	55 (44.3%)	124 (40.3%)	
Smokers	61 (49.2%)	250(81.2%)	0.000
Asthma & COPD	2 (1.6%)	15 (4.9%)	0.115
H/o pulmonary Tuberculosis (TB)	9(7.3%)	54(17.5%)	0.019
Positive family history	6 (4.8%)	2 (0.6%)	0.008

3.2. Pathologic Characteristics

The distribution of histopathologic subtypes in younger age group was found to differ significantly from that in older age group (p=0.000). Younger age group have adenocarcinoma (61.3%) as the most common type followed by squamous cell carcinoma (29.8%), small cell carcinoma (4.8%), others (4.1%). Whereas most common subtype in

older age group were squamous cell carcinoma (58.1%) followed by adenocarcinoma (27.6%), small cell carcinoma (10.7%), others (3.6%)(Table 2). Stage distribution was significantly different between the age groups (p=0.000),younger age group found to have more advanced stage at presentation with 94.4% younger patients presented in stage III or IV compared to 77.3% among older patients (Table 2).

Table 2. Pathological Characteristics.

Histopathology& Stage	Age<60yearN=124	Age≥60yearN=308	p value
Squamous	37 (29.9%)	179 (58.2%)	
Adeno	76 (61.3%)	85 (27.6%)	0.000
Small cell	6 (4.8%)	33(10.7%)	
Others	5 (4%)	11 (3.5%)	
Stage I	1 (0.8%)	2 (0.6%)	
Stage II	6 (4.8%)	68 (22%)	0.000
Stage III	57 (46%)	132 (42.9%)	
Stage IV	60 (48.4%)	106 (34.5%)	

3.3. Treatment Characteristics

There was significant difference (p=0.002) in modalities of treatments received in each age group. Total 75 patients (60.5%) in younger age group received combined modality treatment in the form of surgery, chemotherapy, radiotherapy as per standard protocol, compared to 134 (43.5%) in older age group. Total 12 (3.9%) patients in older age group refused treatment and majorities were of age>80 years, whereas all younger age group received treatment (Table 3).

Table 3. Treatment characteristics.

Treatment	Age<60yearN=124	Age≥60year N=308	P value
CT	46(37.1%)	135 (43.8%)	
RT	03 (2.4%)	27(8.8%)	0.002
CMT	75 (60.5%)	134 (43.5%)	
No treatment	0	12 (3.9%)	

3.4. Survival Characteristics

Median survival was 15 months among younger age group whereas 12 months among older age group (p=0.338). Three year overall survival was found to be 3.2% in younger age group as compared to 6.5% in older age group, survival difference was statistically not significant (p=0.344). The reason behind this may be more aggressiveness of cancer in younger age group, greater comorbidities among older age group, greater proportion in older age group refusing treatment (Table4).

***Table 4.** Survival Characteristics.*

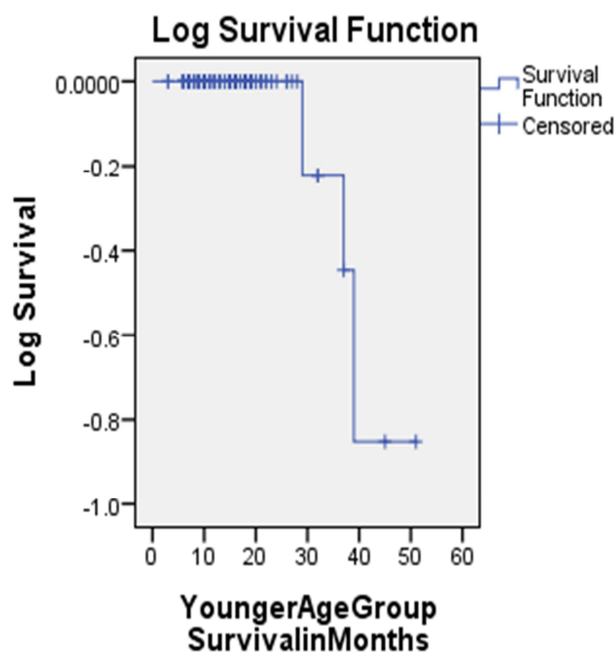| Survival	Age<60(in years)N=124	Age≥60(in years)N=308	P value
Median Survival	15months	12Months	0.338
3year OS	4(3.2%)	20(6.5%)	0.344

***Figure 1.** Log rank survival chart for younger age group.*
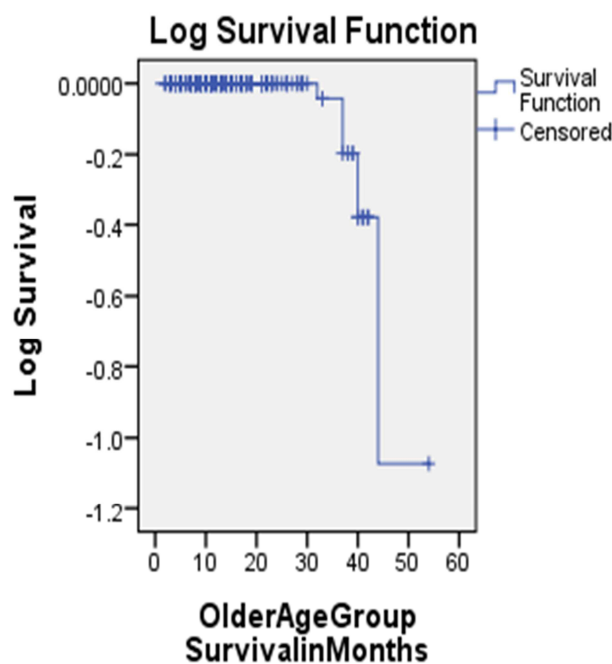

***Figure 2.** Log rank survival chartfor older age group.*

4. Discussion

Due to increasing life expectancy and the increased risk of cancer with ageing, lung cancer is common in elderly individuals. More than half of lung cancer cases are diagnosed in patients aged >65 years [18-20]. The median age at diagnosis of lung cancer is between 64 and 70 years [19, 20].In the present study the median age was 66 years for all age groups, 55 year for younger age group and 70 year for older age group patients. The distribution by gender in the elderly is similar to that in younger patients in the US; whereas, in France, there is a decrease in the male/female ratio with increasing age [21, 22]. In this study, the disease distribution by gender was found to be similar in both younger and older age group. Significantly lesser number of smokers with greater proportion of adenocarcinoma was found among younger age group as compared to older age group, which reflects the successful anti tobacco awareness programme in recent time. Significantly greater positive family history with more advanced stage disease at presentation was found in younger age group, which warrants further clinical studies with cytogenetic analysis to correlate genetic predisposition with early age at presentation and more aggressiveness of the cancer. Toxic events with chemotherapy are more common in elderly patients. Alterations of physiological functions, particularly renal and hematopoietic functions, with aging may explain increased chemotherapy toxicity in elderly patients [19, 23, 24]. Furthermore, elderly patients have more comorbidities than their younger counterparts and thus often take medications that may interfere with the chemotherapeutic drug metabolism. Comorbidities are responsible for an increased mortality in patients even after adjustment for age and stage [19, 25, 26]. In this study proportions of patients receiving combined modality treatment were significantly greater in younger age patients compared to older age patients. Proportions of patients did not go for any active treatment were significantly higher in older age group, probably because of multiple co morbidities, poor performance status and lesser expectation in terms of long term benefit with treatment. Studies performed on elderly patients with various malignancies show that elderly patients benefit from chemotherapy to a similar extent as younger patients, with manageable side effects [27-29].The vast majority of these subgroup analyses demonstrated that the efficacy results are

similar in patients aged<70 years old and in those aged ≥70 years old [28-32].In this study in spite of more advanced stage of presentation of disease in younger age patients and more co morbidities in older age patients, the overall survival was found similar in both the groups.

5. Conclusion

The decreasing number of smokers in younger age group signifies successful anti tobacco awareness programme in the North East part of India since last few decades. Greater incidence of adenocarcinoma, greater positive family history and greater aggressiveness of disease in younger age group needs further clinical studies with genetic analysis to correlate genetic predisposition with disease aggressiveness. Besides histopathology, stage of disease, appropriate treatment protocol, survival of lung cancer patients depend on age at diagnosis, comorbidities, patient's performance status.

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