

RESEARCH ARTICLE

Does Sunlight Exposure Improve Survival in Patients with Non-small Cell Lung Cancer?

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Abstract

Background: Some epidemiological studies reported that sunlight exposure and high vitamin D levels may decrease the morbidity and mortality related to cancer. We aimed to evaluate whether sunlight exposure has an impact on survival in patients with non small cell lung cancer. **Materials and Methods:** A total of 546 patients with NSCLC from two different regions (Kayseri and Adana) differing according to sunlight exposure were analysed retrospectively. **Results:** The median overall survival (OS) rates were 11.6 (CI: 9.50-13.6) and 15.6 months (CI: 12.4-18.8) for Kayseri and Adana, respectively, in all patients (p=0.880). **Conclusions:** There were no differences between groups in terms of OS. While there is strong evidence regarding inverse relationship between cancer incidence and sunlight exposure, it is still controversial whether sunlight exposure is a good prognostic factor for survival in patients with lung cancer.

Keywords: Lung cancer - sunlight - survival - season

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Introduction

Lung cancer is the leading cause of cancer related deaths in both men and women (Jemal et al., 2011; Demirci et al., 2013). Of lung cancers, 85% are non small cell lung cancer (NSCLC) and the 5-year-survival rate is approximately 75% in TNM stage I and it is only 13% in stage IV (Goldstraw et al., 2007; Oguz et al., 2013). Unfortunately, of all patients with NSCLC 15% survive five years. Age, sex, histological type, stage, performance status, some genetic mutations and smoking are known as common prognostic factors (Hoang et al., 2005; Riquet et al., 2007; Albain et al., 2009; Caglar et al., 2009; Alimujiang et al., 2013; Kamsa-Ard et al., 2013; Pan et al., 2013). Some epidemiological studies evaluated whether epidemiologic properties had an effect on mortality or morbidity of cancer (Mutlu et al., 2011; 2013; Fuhrman et al., 2013; Holick et al., 2013). Generally, it was speculated that sufficient solar light exposure and vitamin D level may decrease the morbidity and mortality related to cancer. When it was evaluated some studies about the relationship between geographical or seasonal differences and lung cancer, in a study, it was reported that the lower levels of ultraviolet B irradiance were independently associated with higher incidence rates of lung cancer in

111 countries (Mohr et al., 2008). The other study said that the sun induced vitamin D status at time of lung cancer diagnosis may have a prognostic value (Norton et al., 2012). Turkey include a lot of region those have different climate. Adana city is in the Mediterranean region having a warmer climate, whereas Kayseri is in inner Anatolia having a colder climate. The ratio of sunny days and annual sunlight exposure are much more in Adana than Kayseri city.

In our study, we aimed to evaluate whether there was a difference regarding the overall survival in patients with NSCLC living Kayseri and Adana cities those have different sunlight exposure.

Materials and Methods

Totally of 546 patients with NSCLC from Acibadem Kayseri Hospital and Kayseri Research and Training Hospital in Kayseri and Acibadem Adana Hospital in Adana were analysed retrospectively, using hospital records between 2009-2012. The patients were divided into two groups; Kayseri city having a colder climate (n: 426) and Adana with a warmer climate and more sunlight exposure (n: 120). Staging was made according to the 7th version of TNM lung cancer staging system. Age,

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sex, histological subtypes, stage, comorbidity, smoking status were recorded to Statistical Package for the Social Sciences 16.0 (SPSS Inc., Chicago, IL, USA) (SPSS16.0) statistical software for analysis. Also the date of diagnosis and date of death were recorded in SPSS 16.0.

To determine the characteristics of patients, descriptive statistics (frequency analysis and crosstabs) and independent samples t test were performed. To evaluate the prognostic factors between these groups, a chi-square test was performed. To evaluate overall survival, Kaplan-Meier statistical methods using log rank test were used. The $p < 0.05$ was considered to be statistically significant.

Results

Annual solar light exposure was more intensive in the Mediterranean region than the internal region and the hours of sunshine per day for Kayseri and Adana region were given in Table 1 and shown in Figure 1. The characteristics of patients were given in Table 2. Mean age of patients were 62.5 ± 10.0 and 61.8 ± 10.0 years. for Kayseri and Adana. respectively ($p = 0.461$). The male and female ratio were similar ($p = 0.934$). There was

Table 1. Hours of Sunshine Per Day for Kayseri and Adana (p=0.475)

Months	Kayseri Hours of sunshine per day	Adana Hours of sunshine per day
January	3	5
February	4	5
March	5	6
April	6	7
May	8	10
June	10	11
July	12	11
August	11	11
September	9	9
October	7	7
November	5	6
December	3	5
Mean hours (month)/Total hours (year)	210.9/2531	237.9/2855

Table 2. Demographic Properties

Parameters	Kayseri (n:426)	Adana (n:120)	p value
Age (mean)	62.5 ± 10.0	61.8 ± 10.0	0.461
Sex			0.934
Male	395	111	
Female	31	9	
Histology			0.131
Adenocancer	111	39	
Squamous Cell	186	39	
Other	12	6	
Nonspecified	117	36	
Stage			0.006
1	5 (1%)	5 (4%)	
2	36 (9%)	20 (17%)	
3	189 (44%)	51 (43%)	
4	183 (43%)	41 (34%)	
Unknown	13 (3%)	3 (2%)	
Comorbidity			0.577
Diabetes	24	6	
ASHD	28	8	
Hypertension	26	6	
Others	26	3	
Smoking			0.116
No	322	97	
Yes	344	89	
No	82	31	

no significant difference regarding histology of cancer ($p = 0.131$). comorbidity ($p = 0.577$). smoking status ($p = 0.116$). There was a significant difference for stage between the groups ($p = 0.006$). The ratio of patients with stage 4 was more in Kayseri (43% vs 34%). the ratio of patients with stage 2 were more in Adana (17% vs 9%). The median OS were 11.56 (CI: 9.50-13.62) and 15.60 months (CI: 12.41-18.78) for Kayseri and Adana. respectively. in all patients ($p = 0.880$). In patients with stage 1, 2, 3, the median OS were 19.38 (CI: 15.92-22.84) and 19.41 months (CI: 14.73-27.09) for Kayseri and Adana. respectively ($p = 0.962$). In patients with stage 4, the median OS were 8.11 (CI: 6.32-9.90) and 10.77 months (CI: 5.60-15.94) for Kayseri and Adana. respectively,

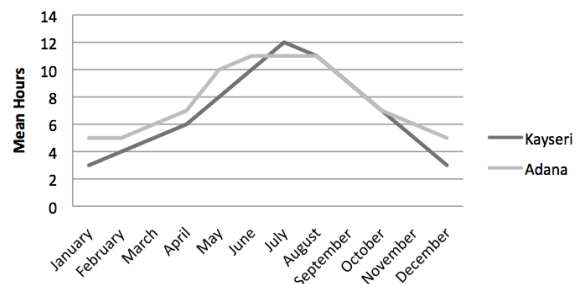


Figure 1. Sunlight Exposure for Kayseri and Adana Regions

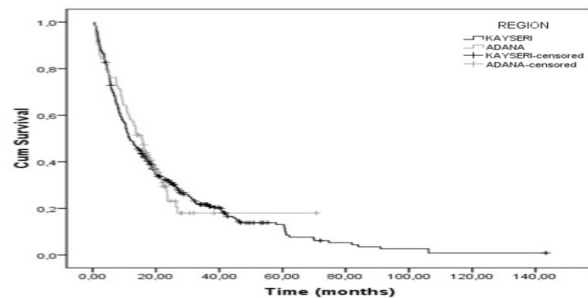


Figure 2. The Overall Survival Curves According to all Patients

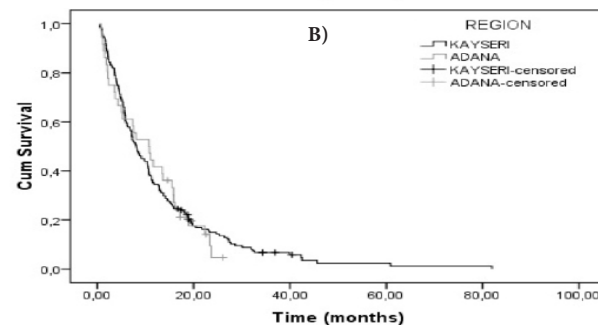
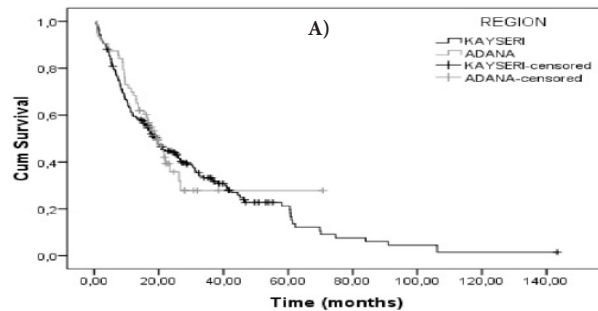


Figure 3. The Overall Survival Curves According to the Patients with A) Local or Locally Advanced Disease; and B) Metastatic Disease

($p=0.849$). The OS curves were shown in Figure 2, Figure 3 and Figure 4 according to all patients, patients with local or locally advanced disease and patients with metastatic disease, respectively.

Discussion

In study presented, we evaluated whether sunlight exposure had an impact on prognosis in patients with NSCLC. According our results, there was no differences between groups in terms of overall survival.

Some *in vitro* studies showed vitamin D3 (1.25-dihydroxyvitamin D3(1.25(OH)2D3)) inhibits lung cancer growth (Nakagawa et al., 2004; Norton et al., 2012). In other *in vitro* studies, it was shown 1α , 25-dihydroxyvitamin D3 24-hydroxylase (CYP24) considering a candidate oncogene was frequently over-expressed and vitamin D receptor (VDR) was modestly down-regulated in lung tumors (Albertson et al., 2000; Anderson et al., 2006). In addition vitamin D3/erlotinib combination resulted in significantly greater growth inhibition than either single agent in both the erlotinib-sensitive HCC827 cell line and the erlotinib-resistant H1975 cell line (Zhang et al., 2012). In order to product vitamin D3 in the body, sunlight exposure is essential. Some studies have evaluated the relationship between sunlight and cancer prognosis. One of them have reported that the patients with NSCLC diagnosed in summer and autumn associated with improved survival compared with that in winter (Lim et al., 2006). In others, it was reported that ultraviolet exposure was related to reduce overall cancer risk (Chen et al., 2010; Yang et al., 2011; Grant, 2013).

Kayseri and Adana cities are similar regarding socioeconomic and dietary habits. Thus in patients with NSCLC living in Kayseri and Adana, the most important environmental factor may be sunlight exposure, especially for production of vitamin D3 considering having an impact on prognosis in patients with cancer. Perhaps we may expect that the patients with NSCLC have higher survival rates in Adana region than Kayseri region because the sunlight exposure is more in Adana region than Kayseri region. Despite of the difference regarding patients with stage IV NSCLC between region (43% vs 34% for Kayseri and Adana region, respectively), we did not find the significant difference between region.

There is strongly evidence regarding inverse relationship between cancer incidence and sunlight exposure through vitamin D3 except for skin cancer. But it is still controversial whether sunlight exposure is a good prognostic factor for overall survival in patients with cancer. In our study we found that there was no difference between patients with NSCLC with differ sunlight exposure. The further studies are warranted to evaluate the relationship between sunlight exposure and mortality of lung cancer.

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