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Review

# More sunlight exposure may improve the overall survival in patients with pancreas cancer

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ABSTRACT

The protective effect of sun exposure on prognosis of cancer and cancer risk was previously reported in some studies except for melanoma and skin cancer. In presented study we aimed to compare the effect of sunlight exposure on prognosis of patients with pancreatic cancer (PC) in two regions with different sunlight exposure. Totally of 139 patients with PC from Akdeniz University from Antalya (n:103) and Kocatepe University (n:36) from Afyon were analyzed retrospectively. Antalya and Afyon state have different sunlight exposure. Two groups were compared in terms of overall survival (OS). The median OS values were 10,9 [95% CI: 7,8–14,0] and 6,9 [95% CI: 3,9–9,9] months for Antalya and Afyon groups, respectively and it was found a significant difference between groups for OS ($p = 0.015$). Also, the region and stage were an independent prognostic factor. In conclusion, the patients with PC had better OS in the region with more sunlight exposure.


## 1. Introduction

Pancreatic cancer (PC) is the eighth and ninth leading cause of cancer deaths in men and women, respectively. In terms of cancer related deaths, PC is included in the top 5 cancers in developed countries.[1] After the age of 45, the incidence of PC rises and is higher in men than women. Hereditary risk factors were determined in 4–16% of patients with PC.[2] In the individuals with non-O blood group, the incidence of PC were significantly higher compared the others with blood group O.[3] Some studies were previously reported that cigarette smoking, diabetes mellitus, cholecystectomy, body mass index $\geq$30 kg/m$^2$, daily intake of red meat, helicobacter pylori, and chronic hepatit B and C infections increase PC risk.[4–9]

The effect of sunlight exposure on prognosis of cancer patients were evaluated by some studies.[10,11] It was generally reported the protective effect of sun exposure on prognosis of cancer and cancer risk except for melanoma and skin cancer. In a study, it was found that ultraviolet B irradiance was independently inversely associated with incidence of PC in men and women.

In presented study we aimed to compare the effect of sunlight exposure on prognosis of patients with PC in two regions with different sunlight exposure.

## 2. Materials and methods

Totally of 139 patients with PC from Akdeniz University (n:103) and Afyon Kocatepe University (n:36) were analyzed retrospectively. Akdeniz University locates in Antalya state which locates in Mediterranean region with more sunlight exposure and a warmer climate while Afyon Kocatepe University locates in Afyon state which locates in inner Anatolia with lower sunlight exposure and a colder climate compared Antalya state. All patients had pancreatic adenocarcinoma confirmed by pathologic review after tru-cut biopsy or surgery. According to the regions where the patients live, the patients with PC were divided into two groups as Antalya and Afyon regions. The hours of sunny days according to region were recorded from the data of Turkish State Meteorological Service. The age, sex, stage, hemoglobin, lactate dehydrogenase (LDH), albumin, calcium and Ca 19-9 levels were recorded to Statistical Package for the Social Sciences 16.0 (SPSS 16.0, SPSS Inc., Chicago, IL, USA) statistical programme. In addition the date of diagnosis, the time of

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progression, the date of death of patients with PC were recorded into the SPSS 16.0 statistical programme.

Statistical analyses were performed using the SPSS software version 16.0. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk's test) to determine whether or not they are normally distributed. According to regions sunny days were compared using two independent samples *t* test. To determine properties of patients with PC, mean, frequencies analysis, two independent samples *t* test and Chi-square tests were performed. The overall survival (OS) was defined as the time from diagnosis to death. The effect of sunlight exposure on OS of patients with PC was investigated using log-rank test. The Kaplan–Meier survival estimates were calculated. P value < 0.05 was considered significant. After univariate analysis, multivariate analysis performed to define the independent prognostic factors for the OS.

## 3. Results

The hours of sunny days of Antalya and Afyon regions were shown in Fig. 1. For the total of 12 months, the hours of sunny days were higher in Antalya than Afyon (p = 0.142).

The mean age of Antalya and Afyon groups were 62,5 ± 10,4 and 66,7 ± 10,7 years, respectively (p = 0.043). It was no found any significant difference regarding sex, hemoglobin and Ca 19-9 levels between groups (p = 0.082, p = 0.140, p = 0.932, respectively). Albumin, LDH and calcium values were significantly higher in Antalya group than Afyon group (p = 0.003, p < 0.001, p < 0.001, respectively). All these results were depicted in Table 1.

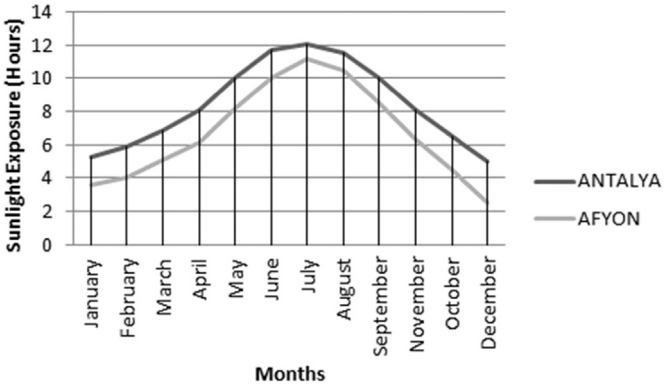


**Fig. 1.** Sunlight exposure according to regions

**Table 1**
Properties of groups

| Parameters | Antalya (n:103) | Afyon (n:36) | P value |
|---|---|---|---|
| Age (mean) | 62,5 ± 10,4 | 66,7 ± 10,7 | 0.043 |
| Sex | | | |
| Male | 76 (73,8%) | 21 (58,3%) | 0.082 |
| Female | 27 (26,2%) | 15 (41,7%) | |
| Stage | | | |
| Stage 1 | 0 | 7 (19,4%) | 0.017 |
| Stage 2 | 9 (8,7%) | 18 (50,0%) | |
| Stage 3 | 22 (21,5%) | 7 (19,4%) | |
| Stage 4 | 70 (67,9%) | 4 (11,1%) | |
| Unknown | 2 (1,9%) | 0 | |
| Hemoglobin | 12,3 ± 1,7 | 11,8 ± 1,6 | 0.140 |
| Albumin | 3,82 ± 0,57 | 3,43 ± 0,75 | 0.003 |
| LDH | 278 ± 153 | 609 ± 228 | <0.001 |
| Calcium | 9,56 ± 0,72 | 8,97 ± 0,78 | <0.001 |
| Ca 19-9 | 1872 ± 6075 | 1968 ± 3462 | 0.932 |

The median OS values were 10,9 [95% CI: 7,8–14,0] and 6,9 [95% CI: 3,9–9,9] months for Antalya and Afyon groups, respectively and it was found a significant difference between groups for OS (p = 0.015). When evaluating local or locally advanced disease, there was also a significant difference between groups. The median OS time of the patients in Antalya had higher than in Afyon (p = 0.001). The median OS values were depicted in Table 2 and shown in Figs. 2 and 3.

In the univariate analysis, region (p = 0.017), stage (p = 0.015), hemoglobin (p = 0.006), albumin (p = 0.003), calcium (p = 0.028) and Ca 19-9 (p < 0.001) levels were found statistically significant (Table 3).

**Table 2**
The OS values for regions

| Stage | Overall survival (median months) | | P value |
|---|---|---|---|
| | Antalya | Afyon | |
| All patients | 10,9 [95% CI: 7,8–14,0] | 6,9 [95% CI: 3,9–9,9] | 0.015 |
| Stage I, II and III | 21,9 [95% CI: 7,8–35,9] | 8,7 [95% CI: 5,5–13,5] | 0.001 |

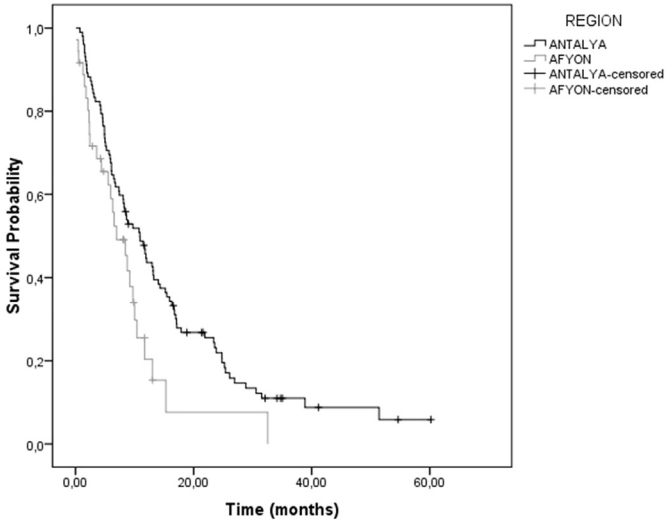


**Fig. 2.** The OS curves according to regions

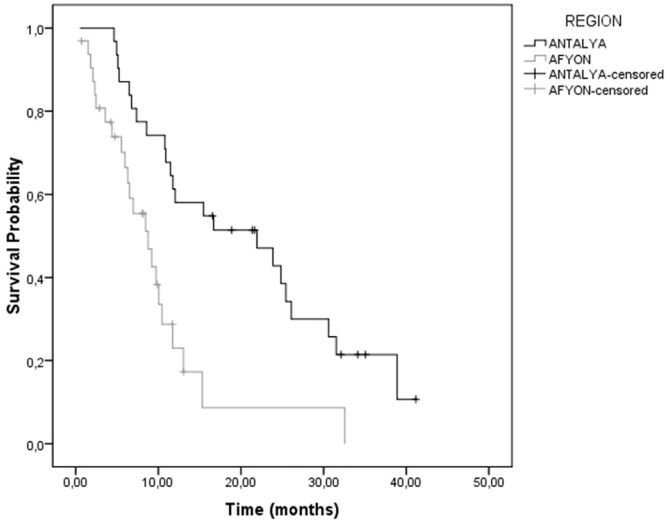


**Fig. 3.** The OS curves according to regions in local or locally advanced disease

**Table 3**
Univariate analysis

| Parameter | P value |
|---|---|
| Age | 0.631 |
| Region | 0.017 |
| Sex | 0.544 |
| Stage | 0.015 |
| Hemoglobin | 0.006 |
| Albumin | 0.003 |
| LDH | 0.303 |
| Calcium | 0.028 |
| Ca 19-9 | <0.001 |

In the multivariate analysis, region and stage were found as independently prognostic factor for OS in patients with PC ($p < 0.001$, $p < 0.001$, respectively) (Table 4).

## 4. Discussion

In presented study, we compared the patients with PC from two different regions according to sunlight exposure in terms of survival unlike a lot of epidemiologic studies those evaluated the cancer incidence according to geographic variation. Antalya and Afyon locate in 36th and 38th north latitudes, respectively, and Antalya state where locates in south and has more sunlight exposure than Afyon state. We found a significantly difference between the OS in the PC patients who located two different regions with different sunlight exposure. The patients with PC from Antalya had significantly higher median OS than others from Afyon, and the region was an independent prognostic factor.

It was known that there are large geographic variations in cancer mortality and the most important risk factors for many types of cancer are environmental.[13] In a review recently reported by Grant WB, it was found that strong inverse correlations with solar UVB for 15 types of cancer: bladder, breast, cervical, colon, endometrial, esophageal, gastric, lung, ovarian, pancreatic, rectal, renal, and vulvar cancer rates.[14] In a study investigated the incidence of PC, it was reported that the incidence of PC was higher in countries with lower UV-B irradiance, with occasional exceptions.[12] Grant WB reported an inverse correlation between mortality rate and UV-B radiation in PC like bladder, esophageal, kidney, lung, rectal, stomach, and corpus uteri and much of the geographic variation in cancer mortality rates in the U.S. can be attributed to variations in solar UV-B radiation exposure.[13] Broscoe et al reported a weaker inverse relationship between solar UV-B exposure and PC mortality.[15] Our results were similar the results in those studies mentioned above.

When evaluating the effect of sunlight exposure on prognosis and incidence of cancer patients, the production of vitamin D via sunlight in the skin seems as a possible explanation. Vitamin D synthesis predominantly depends on the level of UV-B sun radiation that the skin receives. Usually only small amounts of vitamin D are obtained from the diet. Vitamin D have protective effect against the development and progression of different types of cancer.[16] In some studies, it was mentioned that 1,25-dihydroxyvitamin D can inhibit cellular proliferation and angiogenesis, induce cellular maturation and cause apoptosis to prevent malignancy in cancer cell line in vitro.[17,18] Also, vitamin D have beneficial effect including cardiovascular disease, metabolic syndrome, diabetes, asthma, multiple sclerosis, neuropsychological functioning, pregnancy outcomes, and overall mortality.[19–21] In addition, physical activity suggested as one of prevention methods for cancer especially in outside is associated with increased vitamin D levels.[22] A 25-hydroxyvitamin D (25(OH)D) level of less than 20 ng/mL was associated with poor prognosis in patients with PC.[23]

**Table 4**
Multivariate analysis

| Parameter | P value |
|---|---|
| Region | <0.001 |
| Stage | <0.001 |
| Hemoglobin | 0.660 |
| Albumin | 0.064 |
| Calcium | 0.715 |
| Ca 19-9 | 0.169 |

In our study, the region was an independent prognostic factor for OS. These different OS values may be related to the effect of sunlight and vitamin D levels on other prognostic factors. It was previously reported that vitamin D deficiency was associated with infections, malabsorption, autoimmune diseases, renal and hepatic failure, nephrotic syndrome, osteoporosis as cause and consequence.[17] Infection and thromboembolic events are major cause of death in cancer patients. Albumin is known as a negative inflammation marker, and LDH may increase in systemic inflammatory and infectious disease. Also, vitamin D is associated with closely calcium levels. According to our results, albumin and calcium levels were higher and LDH levels were lower in patients with PC who had better survival in Antalya region than Afyon region.

In conclusion, we found that the patients with PC had better survival in the region with more sunlight exposure. The region was an independent factor for OS according to our results. The effects of sunlight exposure on survival of patients with PC should be further examined in a prospective study.

## Conflict of interest

We declare that we have no conflict of interest.

## Financial disclosure

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