



ARAŞTIRMA / RESEARCH

**Distribution of cancer cases in a city of eastern Turkey and the results of survival analysis: a retrospective cohort study**

Türkiye'nin doğusunda bir kentte kanser vakalarının dağılımı ve yaşam analizi sonuçları: retrospektif bir çalışma

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**Abstract**

**Purpose:** The aim of present study was to determine the changes in the incidence of cancer in Bingöl which is in the Nomenclature of Territorial Units for Statistics- 2 (NUTS-2) region, and to perform survival analysis on these patients.

**Materials and Methods:** This is a retrospective cohort study and the data was obtained from the Ministry of Health's Cancer Registry System. We examined the data of 977 cancer cases diagnosed between year 2013 and 2015

**Results:** 28.7% of the patients died during the follow-up period. 30% of all cancers originated from the digestive system. The cancers of lung, stomach, colon, prostate and skin are the mostly seen in the male patients, the cancers of breast, thyroid and skin are the mostly seen in the female patients. The incidence of cancer is increasing over the years and the cancer incidence rate is higher in men. The mean follow-up period was 388 days in died patients and 1541 days in alive patients. The risk of death is increasing in the patients not undergoing surgery (RR = 2.779, HR = 3.048). In addition, the risk of death is decreasing in the patients not receiving chemotherapy (RR = 0.656, HR = 0.340). The risk of death is increasing in the patients with advanced age and the male patients.

**Conclusion:** The incidence of cancer is increasing. Further indepth and wider research is needed to shed more light on these findings

**Keywords:** Cancer, survival, chemotherapy, surgery, radiotherapy

**Öz**

**Amaç:** Bu çalışma ile Türkiye'de Nomenclature of Territorial Units for Statistics 2 (NUTS 2) bölgesinde bulunan Bingöl kentinde kanser insidansında meydana gelen değişimi tespit etmek ve bu hastalarda yaşam analizi yapmak amaçlanmıştır.

**Gereç ve Yöntem:** Bu çalışma bir retrospektif kohort çalışmasıdır. Hastaların verileri Sağlık Bakanlığı Kanser Kayıt sisteminden elde edilmiştir. 2013-2015 yıllarında tanı almış 977 kanser vakasının verileri incelenmiştir.

**Bulgular:** Takip süresi içinde hastaların %28.7'si vefat etmiştir. Bütün kanserler vakalarının %30'u sindirim sistemi kökenlidir. Erkeklerde akciğer, mide, kolon, prostat ve cilt kanserleri kadınlarda meme, tiroit ve cilt kanserleri en fazla görülmektedir. Toplumda yıllar içinde kanser insidansı artmaktadır ve erkeklerde kanser insidans hızı daha fazladır. Ölen hastaların ortalama takip süresi 388 gün yaşayan hastaların ise 1541 gündür. Cerrahi yapılmayan hastalarda ölüm riski artmaktadır (RR=2.779, HR=3.048). Kemoterapi almayan hastalarda ise ölüm riski azalmaktadır (RR=0.656, HR=0.340). Yaşı ileri olan hastalarda ve erkeklerde ölüm riski artmaktadır.

**Sonuç:** Kanser insidansı artmaktadır. Tedavi etkinliğini ve tedavi türlerinin sağkalım üstündeki etkilerini değerlendiren daha uzun ve geniş tabanlı çalışmalar yapılması önerilmektedir.

**Anahtar kelimeler:** Kanser, sağkalım, kemoterapi, cerrahi, radyoterapi

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## INTRODUCTION

Cancer is a generic term for a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to the other organs. Other commonly used terms are malignant tumors and neoplasms. Cancer can affect almost any part of the body and has many anatomic and molecular subtypes each of them require specific management strategies. Cancer is the second leading cause of death globally and is estimated to account for 9.6 million death in 2018<sup>1</sup>. The most common cancer among men are lung, prostate, colorectal, stomach and liver cancer, whereas breast, colorectal, lung, cervix and thyroid cancer are common among women<sup>1</sup>. The current evidence suggest that, about 30% to 50% of cancer deaths could be prevented by modifying or avoiding key risk factors, including avoiding tobacco products, reducing alcohol consumption, maintaining a healthy body weight, exercising regularly and addressing infection-related risk factors<sup>2</sup>. To reduce the significant disability, suffering and deaths caused by cancer, effective and affordable programmes in early diagnosis, screening, treatment, and palliative care are needed. Treatment options may include surgery, medicines and/or radiotherapy; treatment planning should be guided by tumor type, stage and available resources and informed by the preference of the patient. Palliative care, which focuses on improving the quality of life of patients and their families, is an essential components of cancer care. Accelerated action are needed to strengthen cancer care, for achieving global targets to reduce deaths from cancer along with universal health coverage<sup>3</sup>. In this study, we aimed to determine the cancer distribution in Bingöl and to provide result of survival analysis according to the treatment types.

## MATERIALS AND METHODS

A retrospective study was performed on the data of 977 patients diagnosed with cancer in Bingöl City of Turkey, which is in the region of Nomenclature of Territorial Units for Statistics 2 (NUTS 2), between 2013 and 2015. There was no age limitation, and the patients at all age groups were included in the study. The study was approved by local ethical committee of Bingöl (Date:23/01/2019- Number:81966737-929). The data collected from the patients are entered into the CanReg4 program of the Ministry of Health.

CanReg4 is a computer program developed specifically for cancer registry centers by the International Agency for Research on Cancer. The data entered in this program is accessed via the Hospital Information Management System. The data evaluated within the extend of the present study were reached from The Death Notification System of the Ministry of Health and the Hospital Information Management System (HIMS). The information about the age, sex and treatment types of the patients were obtained from HIMS. In addition, the definitive pathologic diagnosis results of the patients were also obtained from HIMS. The follow-up periods of the patients were calculated from the time difference between the date of diagnosis and the date of death recorded in the death notification system. The codes described in the third edition of the International Classification of Disease for Oncology (ICD-O) book published by the World Health Organization were used for the data of histological classification and topographical location. Topographical locations (it defines the tissue in which lesion originates) of the cancers were evaluated in 41 categories. The cancers whose origins were not exactly known, were evaluated in the category of 'Unknown'. These categories were then classified into 9 main categories by considering the organ systems. According to pathology results tumors were evaluated in three classes as benign, in situ carcinoma and malignant.

### Statistical analysis

SPSS 22 program was used in the data analysis. The data of gender, tumor behavior and topographical classification are expressed as percentages. The Kruskal Wallis test, Mann-Whitney U test, Chi-square test and Cox Regression analysis were also used in the analysis of the data. Age, gender, and treatment types determined as the were independent variables in Cox Regression analysis. Final model was constituted using the data of 977 patients with definitive cancer diagnosis. Treatment types were evaluated in three categories as surgery, chemotherapy and radiotherapy. Due to their inadequate count patients receiving hormone therapy and immunotherapy, they were not included in the model. The patients with pathological results as benign and in situ of were excluded in the model. As the information about the stages of the patients could not be reached, it is not possible to include in the model. Hazard ratios of the independent variables included in the model were calculated. Survival analysis graphs of the significant independent variables were also calculated.

**RESULTS**

Pathological examination was performed on the lesions of 1029 individuals due to suspicion of malignancy between 2013 and 2015, it was seen that 977 lesions were malignant. The mean age of the

patients was  $58.73 \pm 16.80$  (min: 1-max: 107). 1.7% of the patients were under 18 years of age, and 98.3% were over 18 years of age. It was seen that 28.7% of the patients died during the follow-up period and 71.3% of them were still alive. The gender and topographic distributions of the organs in which 977 malignant lesions originated are shown in Table-1.

**Table 1. Topographic distribution of all lesions**

Main system	Tissue origin of the lesion	Male n/colon%	Female n/colon%	Total %
Digestive system organs	Mouth	3/0.5	3/0.7	30.2
	Pharyngeal	3/0.5	4/1.0	
	Esophagus	12/2.1	12/2.9	
	Stomach	66/11.7	22/5.3	
	Intestinal	2/0.4	1/0.2	
	Large intestine	47/8.3	41/9.9	
	Rectosigmoid junction	3/0.5	3/0.7	
	Anus-rectum	15/2.7	14/3.4	
	Liver	14/2.5	5/1.2	
	Gallbladder and paths	4/0.7	5/1.2	
	Pancreas	12/2.1	4/1.0	
	Other digestive organs	1/0.2	0/0.0	
Respiratory system	Nasal cavity	0/0.0	1/0.2	11.6
	Larynx	12/2.1	3/0.7	
	Bronchopulmonary	78/13.9	13/3.1	
	Pleura	4/0.7	2/0.5	
Muscle-bone-soft tissue-skin	Bone-joint	4/0.7	0/0.0	11.8
	Skin	65/11.5	38/9.2	
	Peripheral nervous system	1/0.2	0/0.0	
	Peritoneum	0/0.0	3/0.7	
	Soft connective tissue	4/0.7	1/0.2	
Female genitalia and breast	Breast	5/0.9	88/21.3	12.0
	Vulva	0/0.0	1/0.2	
	Cervix-uterus	0/0.0	4/1.0	
	Uterine-ovary	0/0.0	20/4.8	
Male genital	Penis	1/0.2	0/0.0	5.9
	Prostate	52/9.2	0/0.0	
	Testis	5/0.9	0/0.0	
Urinary system	Kidney	24/4.3	10/2.4	8.5
	Bladder	46/8.2	3/0.7	
Central nervous system	Eye	0/0.0	1/0.2	1.0
	Meninges	0/0.0	2/0.5	
	Brain	3/0.5	3/0.7	
	Spinal cord-cranial nerves	1/0.2	0/0.0	
Blood-lymphatic system and thyroid	Thyroid	15/2.7	59/14.3	15.0
	Hematopoietic system	22/3.9	23/5.6	
	Lymph nodes	21/3.7	8/1.9	
Unknown	Undefined	9/1.6	3/0.7	3.6
	Unknown	9/1.6	14/3.4	
Total (n/row%)		563/57.6	414/42.4	977/100.0

When the cancer load is evaluated in terms of both genders, it was found that the digestive system cancers constituted the most load between all

cancers. When the distribution of cancer cases according to gender was considered, it was seen that the approximately 58% of cancers were presence in

the male patients. When we examined the cancer incidence rates according to years, a tendency to increase is seen. It was found that the incidence rate of cancer for all age groups and both genders was 97 per hundred thousand in 2013, 127 per hundred thousand in 2014 and 161 per hundred thousand in 2015 (Figure-1). When the incidences were examined according to genders, the cancer incidence rate of male patients in all age groups was 97 per hundred thousand in 2013, 149 per hundred thousand in 2014 and 184 per hundred thousand in 2015. The cancer incidence rates of female patients were 97, 105 and 137 per hundred thousand, respectively.

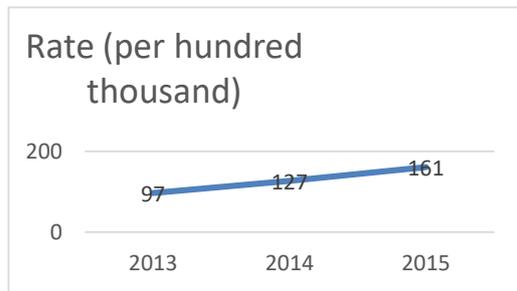


Figure 1. Cancer incidence rates according to years

The mean follow-up period was 388 days in died patients and 1541 days in alive patients. The mean information about the follow-up period of the patients is given in Table-2. The relative risk of mortality was 0.656 in the patients not receiving chemotherapy and 2.77 in the patients not undergoing surgery. The relative risk of mortality is 1.5 times higher in the patients receiving chemotherapy and 2.7 times higher in the patients not undergoing surgery. When the correlation coefficients were examined, it was seen that there was a weak negative correlation between surgical treatment and death risk, and a weak positive correlation between chemotherapy and death risk. The relative risk values of mortality in the patients according to treatment modalities are given in Table-3.

The results of survival analysis performed with the Cox regression model including independent variables as treatment types, gender and age of the patients are given in Table-4. It was found that the fit of Cox Regression model in which the age, sex and treatment types were added as independent variables was good (Omnibus test  $p < 0.001$ ). The reference category in terms of treatment was determined as the

patients receiving a treatment. The dependent variable was defined as whether or not a death status was occurred. It was seen that the variables included in the model except radiotherapy had a significant effect on the survival time.

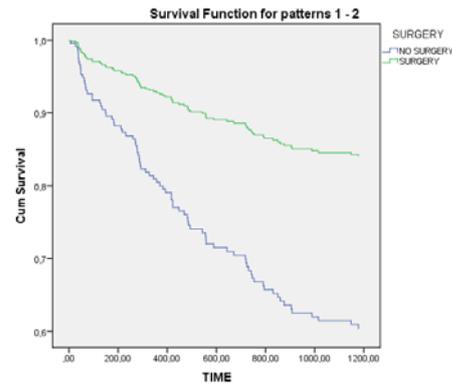


Figure 2. Survival curves according to surgery status

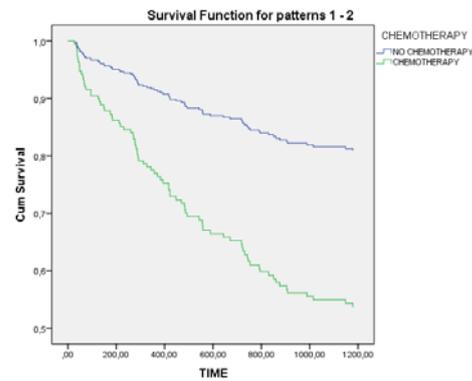


Figure 3. Survival curves according to chemotherapy status.

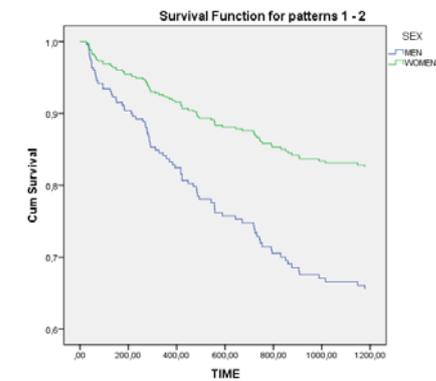


Figure 4. Survival curves according to gender.

It was found that the risk of death increased by 1.021 times in increasing of age, by 2.2 times in the male gender than the female gender, and by 3 times in the patients receiving chemotherapy. It was detected that the risk of death was 3 times lower in the patients

undergoing surgical treatment. The analyses of life curve according to gender and to whether or not to receive chemotherapy and undergo surgical treatment are given in the below graphs.

**Table 2. Average follow-up/lifetime of cancer patients according to type of treatment**

	Average follow-up period (days) ( $\bar{x} \pm S.D.$ )	Median (days)	p
Patient' status			
Lives	1541±315	1495	
Death	388±358	287	
Chemotherapy			
Yes	1037±627	1105	<0.001
No	1369±612	1601	
Surgical			
Yes	1423±515	1590	0.015
No	1072±712	1422	
Radiotherapy			
Yes	1151±555	1151	0.002
No	1296±652	1558	

**Table 3. Relative risks and relationship coefficients according to treatment modalities**

	Relative risk	CI 95%	Phi	p
No Chemotherapy / Chemotherapy	0.656	0.482-0.893	0.139	0.006
No Surgical / Surgical	2.779	2.112-3.655	-0.290	<0.001
No Radiotherapy / Radiotherapy	0.904	0.641-1.275	0.032	0.569

**Table 4. Cox regression survival analysis results**

	B	Hazard ratio	%95 CI	p
Age	0.020	1.021	1.006-1.035	0.005
Sex	0.790	2.203	1.353-3.586	0.001
Chemotherapy	-1.080	0.340	0.210-0.550	<0.001
Surgery	1.114	3.048	1.903-4.882	<0.001
Radiotherapy	0.192	1.212	0.702-2.093	0.490

## DISCUSSION

When the evaluation of all age groups was taken into consideration, it was seen that the malignancies were more common in males and the digestive system cancers were more common according to the organ systems. Gastric, colon, skin, lung, breast, thyroid and prostate cancers are the most frequently seen types of cancer among all cases. When we evaluated the effects of age, gender and treatment types on the death status, it was observed that the risk of death increased with; male, advanced age, receiving chemotherapy and undergoing surgery. It was noted that the incidence rates increase over the years. When the cancer statistics of Turkey are examined, it is seen

that the cancers of the lung-bronchus-trachea, prostate and colorectal, bladder, and stomach are most common in the male patients, whereas the cancers of the breast, thyroid, colorectal, uterus, lung and stomach are most common in the female patients<sup>4</sup>. In our study, it was found that while the cancers of lung, stomach, colon, skin were most common in the male patients, the cancers of breast, thyroid, colon and skin were most common in the female patients. Although our results conform the overall distribution of cancer in Turkey, the incidence of digestive system and the skin cancers are above the national level. This difference can be explained by dietary and occupational habits of regional population. This region is famous for livestock farming. The greater consumption of salted red meat

stored in oil explains the high rates of digestive system cancers in the region. The higher rates of skin cancers is explained by grazing behavior of shepherd during summer. It is thought that the exposure to sun for a long time in the open air increases the risk of skin cancer.

In the years when the study was performed; it was seen that while the cancer rates in the country were decreasing, our study had a found an increasing tendency. It is thought that this tendency was related with increase in life expectancy in the region. In a study performed to evaluate the efficiency of surgical treatment in advanced gastric cancer in China, it was seen that the surgery and the conversion therapy was effective in the patients with stage 2-4. Surgery should be performed when the tumor is maximally responsive to chemotherapy. In addition, palliative resection can be chosen for the patients with pyloric stenosis and complications such as tumor perforation or uncontrolled massive bleeding<sup>5</sup>. In a study comparing the efficacy of surgical treatment in lung cancer by Raman et al., it was seen that the robot-assisted thoracoscopic surgery decreased the complications compared to open surgery. However there was no significant effect on survival<sup>6</sup>. In a retrospective analysis for types of all cancers in Norway were performed, it was found that the risk of death was 1.18 times higher in the male patients and 2.17 time lower in the patients undergoing radical surgery. It was found that the radiotherapy decreased the risk of death in the rectum, lung, breast and prostate cancers<sup>7</sup>. In a study of Molife et al., it was found that the female gender had more advantageous in terms of survival<sup>8</sup>. In an another retrospective cohort study, it was found that there was no significant association in terms of surgery procedures, radiotherapy and chemotherapy between the bladder cancer patients. In addition, it was found that the systemic chemotherapy worsened the prognosis in a few cases, as well as the intravesical chemotherapy was associated with long survival<sup>9</sup>. In a study, the survival analysis for the breast cancer patients was performed and it was seen that the prolongation of the time between surgery and chemotherapy increased the risk of death 3 times<sup>10</sup>. In a metaanalysis, it was shown that the surgery decreased the risk of death in the colorectal cancer patients<sup>11</sup>. In another metaanalysis, it was found that the palliative chemotherapy was associated with a 35% reduction in the risk of death for the patients with colorectal cancer<sup>12</sup>. In a study investigating recurrence of cervical cancer, it was found that whether or not to

receive chemotherapy had no effect on survival<sup>13</sup>. In the female patients with ER (estrogen receptor) positive breast cancer, it was found that the chemotherapy decreased the risk of death by 38%<sup>14</sup>. In our study, it was seen that the risk of death decreased among patients undergoing surgical treatment and increased in the patients receiving chemotherapy. This result may be related to the fact that the surgically treated patients are usually in early stage, the surgical treatment is preferred in the patients with no distant organ metastasis, and the chemotherapy is preferred in the inoperable patients. We also think that the stages of patients that did not add to the model is important in this significance. We think that the higher risk of death in the male patients is associated with the fact that fatal types of cancer are more frequently seen in the male patients. In addition, the inclusion of all types of cancer and all age groups rather than a specific group of cancer patients may be a factor in explaining this difference.

In conclusion, it was found that there was an association between the treatment modalities and survival. It was also found that the risk of death decreased by surgical treatment and increased by chemotherapy. This result is representative of only one city of Turkey for Sub-regional and national level survival indicators border studies are recommended. Cancer registry data provide opportunity for meaningful analysis. However, principal concern with registries is that of making inferences with regard to the quality of data. Since quality standards of Turkish cancer registry have not been reported the above results should be interpreted with caution.

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