RESEARCH ARTICLE

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Evaluating the Relationship between Diabetes and Cancer in a Cohort

Simge Ruhiye Yilmaz Kavcar[1]*, Ayla Acikgoz[2], Gul Ergor[3], Belgin Unal[3]

Abstract

Background/aim: Epidemiological studies indicate that the risk of several types of cancer is high in diabetic patients. The aim of this study is to evaluate the association between diabetes and diabetes related cancers in a cohort design. **Materials and methods:** The baseline survey was conducted as a community screening programme from 2007 to 2009 in a population over 30 years of age. Diabetes definition was based on fasting blood glucose level ≥ 126 mg/dl and self-reported diabetes history. Data on incident cancer cases and pathological types were obtained from the İzmir Cancer Registry between 2007-2013. Odds ratios (OR) were estimated for the relationship between diabetes and diabetes-related cancer types for men and women separately and adjusted for BMI and age. Odds Ratio and 95% confidence intervals were calculated using logistic regression models in IBM SPSS Statistics 24.0. **Results:** Data from 10,375 women (65.4%) and 5,494 men (34.6%) who did not declare any cancer in 2007 were evaluated. The cumulative incidence of diabetes related cancers was 2,293 per 100,000 in men and 1,455 per 100,000 in women. Total diabetes related cancer incidence was higher in diabetics (3,770 per 100,000) than nondiabetics (2,109 per 100,000) in men. **Conclusion:** There was no statistically significant association between diabetes and cancers. The analyses can be repeated in the future when the cohort gets older and more incident cases of cancers occur.

Keywords: Diabetes- cancer- diabetes related cancer

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Introduction

According to the World Health Organization report, diabetes and cancer are the most important non-communicable diseases that threaten human health and development (World Health Organizatin, 2008). Diabetes and cancer are preventable; 80% of type 2 diabetes and more than one-third of cancers can be prevented by reducing risk factors, particularly smoking, malnutrition, physical inactivity and excessive use of alcohol (World Health Organizatin, 2010; IDF Diabetes Atlas, 2015; Okutur, 2015).

The prevalence of diabetes is increasing worldwide. International Diabetes Federation (IDF) estimates that the prevalence of adult diabetes, which was presumed to be 8.8% in 2015 in the world, will increase to 10.4% in 2040 (IDF Diabetes Atlas, 2015).

Due to rapid demographic and epidemiologic transition, Turkey is facing an increase in prevalance of obesity and diabetes. According to the results of Turkish Epidemiology Survey of Diabetes, Obesity and Hypertension (TURDEP-I) which was conducted in 1997-1998 and covered 24,788 people aged 20 years or older, the prevalence of Type 2 diabetes was 7.2% (Satman et al., 2013). In the TURDEP-II survey conducted in 2010, the prevalence of diabetes almost doubled and reached to 13.7% in the Turkish adult population (International Agency for Research on Cancer, 2018). The frequency of diabetes rises with increasing age like many other chronic diseases including cancer, cardiovascular disease and obesity (Prasad et al., 2012). Diabetes was observed in over 25% of men and women older than 65 years of age (Satman et al., 2013; International Agency for Research 45 on Cancer, 2018; Unal et al., 2013).

Cancer is one of the most common global diseases. The estimated number of cancer cases was approximately 18.1 million and cancer deaths were 9.6 million in 2018 (International 48 Agency for Research on Cancer, 2018). The most common types of cancer in 2018 were lung cancer and breast cancer (approximately 2.1 million cases for each types, 11.6%), colorectal cancer (1.8 million cases, 10.2%), prostate cancer (1.3 million cases, 7.1%) and stomach cancer (1.0 million cases, 5.7%) (International Agency for Research on Cancer, 2018). The five most common types of cancer in men are lung cancer, prostate cancer, colorectal cancer, stomach cancer, and liver cancer. In women, the most common types of cancer are breast cancer, colorectal cancer, lung cancer,

*[1]Department of Endocrinology and Metabolic Diseases, Dokuz Eylul University Hospital, Balcova, İzmir, Turkey. [2]Vocational School of Healthcare, Dokuz Eylul University, Balçova, İzmir, Turkey. [3]Department of Public Health, Faculty of Medicine, Dokuz Eylul University, Balçova, İzmir, Turkey. *For Correspondence: yilmazsimge@yahoo.com*

cervical cancer and stomach cancer (Giovannucci et al., 2010; World Health Organizatin, 2017).

The cancer incidence and mortality have been increasing in Turkey as it has been in many developing countries. According to latest data from Turkey Cancer Statistics, the first five most common types of cancer in women are breast cancer (43.8 per 100,000), thyroid cancer (21.7 per 100,000), colorectal cancer (14.4 per 100,000), uterine cancer (10.0 per 100,000) and lung cancer (9.0 per 100,000), relatively. In men, the first five most common types of cancer are lung cancer (52.5 per 100,000), prostate cancer (33.1 per 100,000), colorectal cancer (23.1 per 100,000), bladder cancer (20.2 per 100,000) and stomach cancer (14.2 per 100,000) (Cancer Report, 2015).

The first finding of the relationship between diabetes and cancer was obtained in 1934 by detecting the frequency of pancreatic cancer higher in people with Diabetes Mellitus (DM) when compared to people without DM (Giovannucci et al., 2010). In a study published in 2000, 8-18% of cancer patients were found to have diabetes (Habib and Rojna, 2013). Then, an increase in the risk of various solid and hematologic malignancies in patients with DM was identified in clinical and epidemiological investigations (Gong et al., 2021). Although the risk of pancreatic cancer, liver cancer, and endometrial cancer was the highest, the frequency of colorectal cancer, breast cancer, gynecological cancers, kidney and bladder tumors were also high in people with DM (Habib and Rojna, 2013). However, the risk of prostate cancer was lower in people with DM (Unal et al., 2013). According to another study, the relative risk of liver cancer, pancreatic cancer and endometrial cancer in diabetes-related cancers was 2.0-2.5, while it was indicated as 1.2-1.5 for breast cancer, colon cancer and bladder cancer (Xu et al., 2014). It has been reported that hyperglycemia and hyperinsulinemia, which are diabetes-associated pathophysiological mechanisms, are associated with increased risk of cancer through the effect of inflammation on neoplastic processes (Sun and Kashyap, 2011; Garg et al., 2014). Although there are many epidemiological data, there are still questions about the main causes of DM and cancer. It is not clear whether the increased cancer frequency seen in diabetics is due to the similar pathogenetic features of both diseases. On the other hand, it seems that like obesity, hyperlipidemia, insulin resistance and macro and microvascular complications associated with diabetes are the main responsible factors for the risk of developing cancer. It has not yet been disclosed (Okutur, 2015; Giovannucci et al., 2010; Danker et al., 2012).

In this study, we aimed to evaluate the association between diabetes and cancer incidence 88 by determining the incidence of diabetes-related cancers at the end of the 7-years follow-up period in men and women aged 30 years and older who participated in the baseline evaluation of Balçova's Heart (BHS) Study.

Materials and Methods

The baseline cross-sectional Balcova Heart Study (BHS) was conducted with the cooperation of Dokuz Eylul University and Balçova Municipality in 2007 in Izmir (Ergor et al., 2012). The people who participated in the baseline survey were followed up for newly diagnosed cancer between 2007 and 2013. People who initially reported a cancer history (n=139) were excluded from the follow up. In total 1643 people with diabetes and 14,226 people without diabetes were followed-up for diabetes-related cancer development in the following six years (Figure 1).

The dependent variable of the study is the presence of cancer, which is thought to be associated with diabetes. These cancers were breast cancer, ovarian cancer, liver cancer, bladder cancer, pancreatic cancer, uterine cancer, and colorectal cancer. Records of Izmir Cancer Monitoring and Control Center (KIDEM) were used to detect the newly diagnosed cancer cases between the years of 2008 and 2013. KIDEM cancer registry includes all cancer cases diagnosed in all public and private hospitals and private laboratories in Izmir (Eser et al., 2010).

Data Collection

The baseline data on sociodemographic characteristics (age, gender, educational status, social security status, employment status, marital status), lifestyle and dietary habits (dietary habits, smoking, physical activity), medical condition of the person (presence of chronic disease, weight, height, BMI) were collected using a questionnaire by face- to- face interviews. Blood samples were taken after at least 8 h of overnight fasting. Fasting blood glucose level was determined in the DEU Hospital Laboratory with Abbott Architect c16000 system on the day of blood collection.

Definition and criteria of variables

The presence of diabetes was determined as the self reported doctor diagnosed diabetes or a fasting blood glucose level over 126 mg/dl detected during the survey. The presence of doctor diagnosed chronic disease history was determined in the baseline survey the BHS project. Body mass index (BMI) of people were calculated as weight (kg) divided by height(m)^2 and classified according to World Health Organization (WHO) definition (<18.50 kg/m^2: underweight, 18.5-24.9 kg/m^2: normal, 25.0-29.9kg/m^2: overweight, >30.0kg/m^2: obese (WHO Expert Consultation, 2004).

Educational status was based on the latest school graduated and grouped as illiterate, literate, primary school graduate, secondary school graduate, high school graduate and postgraduate. Health security status was defined as Retirement Fund, Bağ-Kur, Social Insurance Institution (SSK), private insurance, green card (a health card for uninsured people in Turkey) and no health insurance. Employment status was determined with using the answer to the question "What is your job?" was recorded open-ended. Dietary habits were evaluated using responses to questions on bread types, cooking oil types, salt use, reading food labels, consumption of vegetables and fruits (Ergor et al, 2012). Data on alcohol consumption, smoking, physical activity were also collected using questionnaire (Ergor et al, 2012). Smoking status was defined as never smoker/current smoker/ex-smoker.

Current smokers were those reported smoking every day or some days at the time of interview. Nonsmokers were defined as those who never had smoked. Ex-smokers were those who reported smoking during their lifetime, but currently did not smoke. Individuals were classified as moderately active if they undertake activity on at least 5 days/week and do at least 30 min of moderate-intensity activity and/or walking (Craig et al., 2003).

Statistical analyses

The cumulative 6 years incidence of diabetes-related cancer types (per 100,000) was calculated by dividing the number of new cancer cases to the baseline healthy population (Portney, 2000). The incidence rates were presented by gender. The categorical variables were presented in numbers and percentages, while the continuous variables were presented as mean ± standard deviation. In statistical analysis, the relationship between categorical variables and cancer was analyzed using chi-square test and the statistical significance level was accepted as $p<0.05$. Odds ratios (OR) were estimated for the relationship between diabetes and diabetes-related cancer types for men and women separately and adjusted for BMI and age. Odds Ratio and 95% confidence intervals were calculated using logistic regression models in IBM SPSS Statistics 24.0.

Results

There were statistically significant differences in the initial characteristics, gender, age and other sociodemographic characteristics of people with diabetes (n=1,643) and without diabetes (n=14,226). People with diabetes were older in age and had lower educational status. Participants with diabetes had higher prevalence of smoking history, obesity and sedentary life style and consumed less portions of vegetable or fruits compared to people without diabetes ($p=0.02$ for gender, $p <0.001$ for others, Table 1).

In total there were 277 diabetes-related cancer cases between the years of 2007 and 2013 in Izmir. The six-years cumulative incidence rate of total diabetes-related cancers was 1,746 per 100,000 in the whole group; incidence of diabetes-related cancer was slightly higher in people with diabetes (2,313 per 100,000) compared to those without diabetes (1,680 per 100,000) ($p=0.06$). Six-years cumulative incidence rates of diabetes-related cancers were presented for the study group with and without diabetes, in men and women in Table 2a-2b.

In men the six-years cumulative incidence rate of total diabetes-related cancers was 2,293 per 100,000 and the incidence of diabetes-related cancer was higher in people with diabetes (3,770 per 100,000) compared to those without diabetes (2,109 per 100,000) ($p=0.01$). In women the six-years cumulative incidence rate of total diabetes-related cancers was 1,455 per 100,000 and there was no statistically significant difference between women with diabetes (1,452 per 100,000) and women without diabetes (1,456 per 100,000) ($p=0.99$). Prostate cancer in men and liver cancer in women were significantly higher in people with diabetes than in people without diabetes ($p= 0.03$, $p<0.01$ respectively) (Table 2a-2b).

The crude, BMI and age adjusted ORs of diabetes for the diabetes-related cancers in men were presented in Table 3a. Overall, the OR of diabetes for diabetes related cancers was 173 1.82 (95% CI:1.15-2.89) when adjusted for BMI the association was similar (OR=1.84, 95% CI:1.14-2.96). However, when adjusted for BMI and age, the OR of diabetes weakened and lost statistical significancy (OR= 1.21, 95% CI: 0.75-1.97). Diabetes OR was 1.87 (95% CI: 1.06-3.30) for prostate cancer when adjusted by BMI the association was similar (OR=1.86, 95% CI:1.04-3.34). However, these significant associations between diabetes and prostate cancer disappered when adjusted for BMI and age, OR 1.25 (95% CI: 0.69-2.27). Odds ratios calculated

Table 1. Initial Characteristics of People with and without Diabetes in the BHS Study Group, 2007.

	With Diabetes n=1643 n (%)	Without Diabetes n=14226 n (%)	p
Gender			0.02
Male	610 (37.1)	4884 (34.3)	
Female	1033 (62.9)	9342 (65.7)	
Age groups			<0.001
30-44	126 (7.7)	4858 (34.2)	
45-59	605 (36.8)	5247 (37.0)	
60-74	739 (45.0)	2725 (19.1)	
75 and older	173 (10.5)	779 (5.5)	
Educational status			<0.001
Illiterate	176 (10.7)	747 (5.3)	
Literate	124 (7.5)	455 (3.2)	
Primary School	834 (50.8)	5994 (42.1)	
Secondary School	151 (9.2)	1571 (11.0)	
High School	220 (13.4)	3259 (22.9)	
University	124 (7.5)	1844 (13.0)	
Smoking			<0.001
Yes - often	308 (18.8)	4615 (33.2)	
Yes - sometimes	33 (2.0)	453 (3.3)	
Quitted	462 (28.2)	2655 (19.1)	
No	835 (31.0)	6174 (44.4)	
Body Mass Index			<0.001
Underweight	5 (0.3)	241 (2.2)	
Normal	144 (9.0)	2265 (20.8)	
Overweight	551 (34.5)	4332 (39.8)	
Obese	898 (56.2)	4057 (37.2)	
Vegetable or fruit portion per day			<0.001
<5	1026 (64.8)	9351 (70.3)	
≥5	557 (35.2)	3960 (29.7)	
Physical Activity			<0.001
High	27 (1.7)	574 (4.3)	
Medium	488 (31.5)	4832 (36.6)	
Low	520 (33.6)	5059 (38.3)	
Sedentary	514 (33.6)	2746 (20.8)	

Table 2a. Six Years Diabetes-Related Cancer Incidence Rates in Men with and without Diabetes (per 100.000)

	Six years Cumulative Incidence Rate						
	Total (n=5494)		With Diabetes (n=610)		Without Diabetes (n=4884)		p
Types of diabetes related cancer	n	per 100.000	n	per 100.000	n	per 100.000	
Prostate	80	1456	15	2459	65	1331	0.03
Bladder	16	291	3	492	13	266	0.33
Colorectal	19	346	3	492	16	328	0.52
Pancreatic	5	91	0	0	5	102	0.43
Liver	6	109	2	328	4	82	0.08
Total Diabetes-related cancers in men	126	2293	23	3770	103	2109	0.01

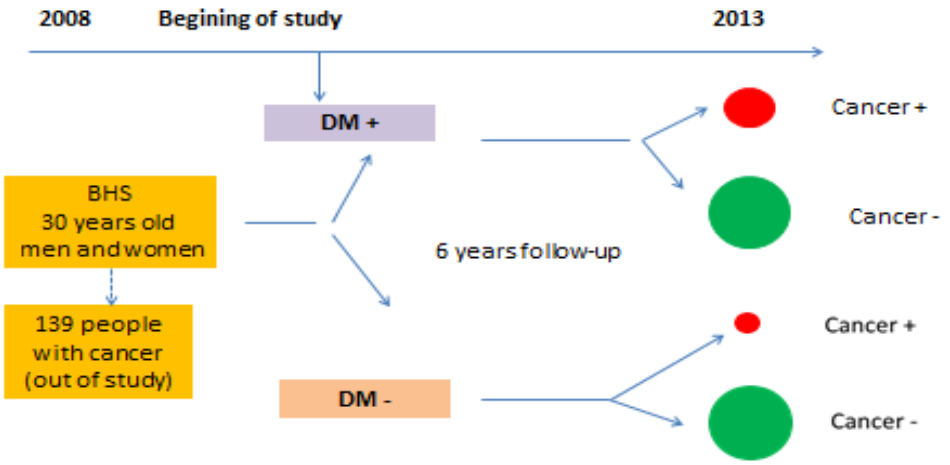

Figure 1. Balçova Heart Study Cohort. Evaluating the relationship between diabetes and cancer in a cohort

for bladder, liver, pancreatic and colorectal cancers were not statistically significant.

The crude, BMI and age adjusted ORs for diabetes and diabetes-related cancers in women were presented in Table 3b. Overall the OR of diabetes for diabetes related cancers was 0.99 (95% CI:0.58-1.70) when adjusted by BMI and BMI, age the association was weakend and became statistically insignificant (OR=0.86, 95%CI:0.48-1.51, OR=0.69, 95%CI:0.38-1.23). Odds ratios calculated for the other types of cancer were not statistically significant.

Discussion

In this study, 1,643 people with diabetes and 14,226 people without diabetes who participated in the baseline cross-sectional survey of the BHS Project were followed up for 6-years for development of diabetes-related cancers using the data from the population-based Izmir Cancer Regisity (KIDEM). According to gender, the cumulative incidence of total diabetes-related cancer was found to be 2,293 per 100,000 in men and 1,455 per 100,000 in women. The first three most common types of cancer in men are prostate cancer, colorectal cancer, and bladder cancer. The first three most common types of cancer in women are breast cancer, colorectal cancer, and uterine cancer. Prostate cancer was significantly higher in diabetics men than non-diabetic men. Total diabetes related cancers were more common in diabetics than non diabetic people, in men.

In this study, statistically significant relationship

Table 2b. Six Years Diabetes-Related Cancer Incidence Rates in Women with and without Diabetes (per 100.000)

	Total (n=9342)		With Diabetes (n=1033)		Without Diabetes (n=10375)		p
Types of diabetes related cancer	n	per 100.000	n	per 100.000	n	per 100.000	
Breast	84	810	9	871	75	803	0.82
Bladder	9	87	1	97	8	86	0.91
Colorectal	20	193	1	97	20	193	0.46
Pancreatic	7	67	0	0	7	75	0.38
Liver	1	10	1	97	0	0	<0.01
Uterine	11	106	1	97	10	107	0.92
Servics	10	96	1	97	9	96	0.99
Ovarian	9	87	1	97	8	86	0.91
Total Diabetes-related cancers in women	151	1455	15	1452	136	1456	0.99

Tablo3a. Diabetes and Diabetes-Related Cancer Relationship in Men, OR (95%Cl)

Types of cancer	All Diabetes-related cancers		Prostat cancer		Bladder cancer		Liver cancer		Pancreatic cancer		Colorectal cancer	
	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)
DM-	4781	103	4819	65	4871	13	4880	4	4879	5	4868	16
DM+	587	23	595	15	607	3	608	2	607	0	607	3
OR	1.82		1.87		1.85		4.01		-		1.5	
(95% CI)	(1.15-2.89)		(1.06-3.30)		(0.53-6.52)		(0.73-21.96)				(0.44-5.18)	
OR*	1.84		1.86		1.89		3.86		-		1.41	
(95% CI)	(1.14-2,96)		(1.04-3.34)		(0.51-6.94)		(0.63-23.65)				(0.40-5.08)	
OR**	1.21		1.25		1.12		2.55		-		0.97	
(95% CI)	(0.75-1.97)		(0.69-2.27)		(0.30-4.18)		(0.40-16.23)				(0.27-3.57)	

#, For OR's the reference is the without DM group; *, BMI adjusted; **, BMI age adjusted

was found between diabetes and the incidence of all diabetes-related cancers in men. Many studies have shown that the presence of diabetes increases the risk of cancer (Giovannucci et al., 2010). The mechanism of the relationship between diabetes and cancer has not yet been fully explained. However, there is a strong evidence that insulin resistance and its concomitant hyperglycemia may cause this condition. It has been suggested that hyperglycemia caused by the formation of a possible mitogenic effect when insulin is linked to insulin-like growth factor-1 (GLP-1) causes carcinogenesis by increasing oxidative stress (Tangvarasittichai, 2015). Meta-analyses have shown that the risk of breast cancer, endometrial cancer, bladder cancer, liver cancer, colorectal cancer, and pancreatic cancer increases in the presence of diabetes and however, the risk of prostate cancer decrease l with diabetes (Noto et al., 2011). In this study, we found that prostate cancer was significantly higher in diabetics when compared with non-diabetics. However, after adjusting to age this association disappeared. One reason for the different results may be that this meta-analysis includes 12 cohort studies with larger study populations and longer follow up times compared to our study.

In this paper, the incidence of cancer in diabetic men was found to be higher than in non-diabetic men. Especially prostate cancer is more common in diabetic men. In diabetic and non-diabetic women, the incidence of cancer was similar. In a cohort of 383,799 people, 23,358 people were diabetics and 1,464 of those people had cancer. They were found to have a high risk of liver cancer, pancreatic cancer, colorectal cancer, bladder cancers for both genders; kidney cancer and uterine cancers were found to pose risk only in women (Ballotori et al., 2017). According to the results of 12 cohort studies and a meta-analysis in which there were 257,222 diabetic people, the incidence of cancer determined was approximately 7% higher in diabetics (Giovannucci et al., 2010). According to another meta-analysis based on result from 29 cohorts and 152,091 diabetic people, the risk of cancer was found to be approximately 3% higher (Noto et al., 2011).

Cancer incidence rates are generally higher in men. Although certain cancers are gender-specific, cancer is more common in men than in women as it can be understood from the results of the studies and reports (Turkey Ministry of Health, 2016). In this study, diabetes-related cancers were also significantly higher in men than women.

Studies have reported that the increased IGF-I level in women diagnosed with breast cancer at a relatively young age (below 50 years) poses a twofold risk of developing breast cancer. Subsequent studies have reported a moderate increase in the risk of breast cancer 231 approximately 30% in women diagnosed with breast cancer after age 50 (Boyle and Levin, 2008; Peairs et al., 2011). In this study, no relation was found between diabetes and breast cancer.

Two case-control studies have reported that the presence of increased concentrations of IGF-I in young women (at premenopausal or menopausal age) showed an increased risk of ovarian cancer (Peairs et al., 2011, The

Tablo 3b. Diabetes and Diabetes-Related Cancer Relationship in Women, OR (95%Cl)

Types of cancer	All Diabetes-related cancers		Breast cancer		Bladder cancer		Liver cancer		Pancreatic cancer		Colorectal cancer		Ovarian cancer		Uterine cancer	
	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)
DM-	9206	136	9267	75	9334	8	9342	0	9334	8	9323	19	9334	8	9332	10
DM+	1018	15	1024	9	1032	1	1032	1	1033	0	1032	1	1032	1	1032	1
OR	0.99		1.09		1.13		-		-		0.47		1.13		0.92	
(95% CI)	(0.58-1.70)		(0.54-2.17)		(0.14-9.04)						(0.06-3.55)		(0.14-9.04)		(0.11-7.07)	
OR*	0.86		0.89		1.02		-		-		0.44		1.02		0.46	
(95% CI)	(0.48-1.51)		(0.42-1.89)		(0.12-8.93)						(0.05-3.51)		(0.12-8.75)		(0.55-3.89)	
OR**	0.69		0.74		0.63		-		-		0.32		1.24		0.4	
(95% CI)	(0.38-1.23)		(0.35-1.60)		(0.07-5.36)						(0.04-2.53)		(0.13-11.46)		(0.04-3.39)	

#, For OR's the reference group is the without DM group; *, BMI adjusted; **, BMI, age adjusted

Endogenous Hormones and Breast Cancer Collaborative Group, 2010). In this paper, the frequency of ovarian cancer in diabetic women was found to be similar to non-diabetic women.

Findings on the relationship between circulating endogenous IGF-I concentrations and prostate cancer risk are increasing in the epidemiological studies (Peairs et al., 2011). In this study, the frequency of prostate cancer was higher in diabetic people than in non-diabetic people.

Studies have shown that there is a positive relationship between diabetes and pancreatic cancer. The critical question is whether diabetes is the cause or outcome of pancreatic cancer ("reverse causality") and it has not been clarified yet (Okutur, 2015). The subgroup analysis of the meta-analysis has indicated that the relationship between diabetes and pancreatic cancer is independent of body mass index (BMI) and insulin resistance.

However, a recent meta-analysis has revealed a relationship between BMI and risk of pancreatic cancer (Okutur, 2015). No relationship was found between the presence of diabetes and pancreatic cancer in this study. This may be because of the fact that the duration of follow up was relatively short and there were no cases of pancreatic cancer reported in those periods.

The relationship between diabetes and the incidence of liver cancer was shown in a meta-analysis of 25 cohort studies published in 2012 (Wang et al., 2012). In our study, a positive 255 but notsignificant relationship was found between diabetes and liver cancer in men.

Endometrial cancer is associated with high insulin concentration in blood and high concentration of biologically available sex steroids and insulin resistance. Type 2 and Type 1 diabetics have been associated with endometrial cancer (Boyle and Levin, 2008). In a meta-analysis which includes 15 cohort studies of diabetic women, the risk was 1.81 (%95 confidence interval [CI]: 1.38-2.37) (Danker et al., 2012). In our study, uterine cancer was not associated with diabetes.

As in other cancer types, hyperinsulinemia and urinary infections that are common in diabetic patients are thought to be the mechanisms responsible for the increase in the risk of bladder cancer. In this study, OR of diabetes was not statistically significant for bladder cancer in men or women.

In conclusion, the total six years cumulative incidence of diabetes-related cancer was 2,293 per 100,000 in men and 1,455 per 100.000 in women in Balcova Distrcit. Diabetes related cancer incidence was significantly higher in men with diabetes than without diabetes. The positive relationship between diabetes and cancer in the men should be examined to clarify the possible mechanism of the relationship in prospective studies investigating common risk factors and possible links.

Author Contribution Statement

The authors confirm contribution to the paper as follows: study conception and design: Yılmaz S and Unal B; data collection: Yılmaz S., and Acikgoz A; analysis and interpretation of results: Yılmaz S and Unal B; draft manuscript preparation: Yılmaz S and Unal B. All authors reviewed the results and approved the final version of the manuscript'.

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Study Implication

This is the first cohort study conducted in Turkey, which investigates the relationship between diabetes and cancer. The population based KIDEM cancer registry provided a unique opportunity to study the diabetes and cancer association. The cancer cases were based on pathological diagnosis rather than self report. The data on baseline characteristics, diabetes history were collected by the trained interviewers and fasting blood glucose was measured in the same laboratory and (Ergor et al., 2012).

In the study some limitations were observed. Firstly, the main limitation could be the relatively small sample size for some cancers with low incidence rates. Secondly, the follow-up time was relative short. These limitations could result in insignificant associations between diabetes and diabetes related cancers in our study.

Availability of the data

All the data are included within the article.

Scientific Approval

The proposal of the study was reviewed and approved by Non-Invasive Research Ethics Board of Dokuz Eylul University Medical Faculty.

Ethical Approval

Ethical approval for the study was obtained from the Non-Invasive Research Ethics Board of Dokuz Eylul University Medical Faculty (20.03.2014; protocol number, 69-SBKAEK).

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Conflict of Interest

The authors have no conflicts of interest to disclose.

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