Clinical research

The relation between smoking and smoker timing and diabetic complications in type 2 diabetes mellitus patients

Huseyin Cetin[1], Mehmet Agin[2], Yusuf Kayar[3], Iskender Ekinci[4], Fatih Borlu[1], Yuksel Altuntas[1]

[1]Department of Internal Medicine, Sisli Etfal Education and Research Hospital, Istanbul, Turkey
[2]Department of Pediatrics, Van Education and Research Hospital, Van, Turkey
[3]Department of Internal Medicine, Van Education and Research Hospital, Van, Turkey
[4]Department of Internal Medicine, Kanuni Education and Research Hospital, Istanbul, Turkey

Corresponding author:
Mehmet Agin
Department of Pediatrics
Van Education
and Research Hospital
Van, Turkey
Phone: +90 5068011083
E-mail: drmehmet47@yahoo.com

Submitted: 11 August 2018
Accepted: 6 October 2018

Arch Med Sci Civil Dis 2018; 3: e95–e102
DOI: https://doi.org/10.5114/amscd.2018.80298

Abstract

Introduction: Active and passive smoking are the main causes of preventable diseases and deaths worldwide, and pose a serious public health problem. In many studies, it has been shown that smoking increases the risk of type 2 diabetes mellitus (DM) development and is associated with bad glycemic control and development of diabetic complications in diabetic patients. Our aim in the present study was to examine the relation between smoking and diabetic complications in type 2 DM patients.
Material and methods: A total of 757 patients who were followed up with type 2 DM diagnosis were included in the present study. The demographic and anthropometric features, diabetic complications, smoking history and when the patients quit smoking were recorded. The relation between smoking and diabetic complications was also investigated.
Results: A total of 54.8% (415 patients) of the patients did not smoke; 12% (91 patients) had quit smoking; and 33.2% (251 patients) were still smoking. There was a statistically significant relation between smoking and male gender, waist circumference, glycated hemoglobin (HbA_{1c}) level, lifestyle, drug compliance, hypertension and diabetic complications. There was a statistically significant relation between smoking quitting period and male gender, HbA_{1c} level, waist circumference, lifestyle, drug compliance and diabetic complications.
Conclusions: A significant relation was observed between smoking and microvascular and macrovascular complications. It was shown that after quitting smoking, bad glycemic control and complications diminished in time. Smoking in diabetic patients is the most important risk factor that may be changed.

Key words: diabetes mellitus, smoking, ex-smoker timing.

Introduction

Diabetes mellitus (DM) is a chronic and metabolic disease requiring continuous medical care, and is the most common endocrine disease in the whole world because of defects in insulin deficiency or the insulin effect in which the organism cannot make use of carbohydrates, fats and proteins [1]. In 2012, there were 371 million people with diabetes in the whole world, 4.8 million people lost their lives because of DM, and about

471 million US dollars were spent on diabetic patients. It is estimated that there will be a total of 552 million diabetic patients in 2030 [2]. It is also estimated that in 2014, average health expenses per diabetic individual will vary between $1.583 and $2.842 in the whole world. The estimated annual global health expenses related to diabetes range from $612 billion to $1099 billion [3]. While in the first Turkey Diabetes, Hypertension, Obesity and Endocrinology Diseases Prevalence (TURDEP) Study, which was conducted in the 1998–1999 period, the DM prevalence in our country was determined as 7.7%, it was found that this rate increased up to 13.7% in the TURDEP II Study, which was conducted in 2010 [4, 5].

It is known that DM causes very serious complications such as coronary artery disease, cerebrovascular events, extremity pathologies, hypertension, nephropathy, retinopathy and neuropathy [6]. Good medical care and individual management are necessary to prevent acute complications and to reduce long-term complications of the disease [7].

Throughout the world, active and passive smoking are the main causes of morbidity and mortality which may in fact be prevented, and pose an important public health problem in both adults and children. Tobacco use causes 5.4 million deaths on an annual scale. If serious precautions are not taken in this respect, this number will increase; and it is predicted that it will reach around 8 million in 2030 [8].

According to the Global Tobacco Products Report prepared by the World Health Organization (WHO) for the year 2007, Turkey ranks 10th among countries where cigarettes are consumed at the highest rate; and in the report that was released in 2008, it was reported that 31.2% of the adult population smoked: 47.9% of men and 15.2% of women [9].

In many studies conducted previously, it has been shown that smoking increases the risk of developing type 2 DM, and is also associated with bad glycemic control and diabetic complication development in diabetic patients. In addition, tobacco smoking has also been found to be associated with earlier development and progression of microvascular and macrovascular complications in DM patients [10–12]. The primary purpose of our study was to examine the effects of smoking on chronic diabetes complications in type 2 DM patients by considering their lifestyles; and the second purpose was to examine how the DM and its complications were affected after quitting smoking.

Material and methods

A total of 757 patients, who were followed up with type 2 DM diagnosis in the Internal Diseases Clinic between 18 and 70 years of age, were included in this study. Volunteering patients who were 17 years of age or older, diagnosed with type 2 DM and who signed the consent form for participation to in study were included in the present study. Patients who were under 17 years of age, those who had type 1 DM, pregnancies, and those who did not volunteer to participate to the study although they met the inclusion criteria were excluded from the study. After the informed consent forms were obtained from the participants, their demographic and anthropometric characteristics (age, gender, duration of disease, type of disease (type 1 DM, type 2 DM), hemoglobin glycated (HbA_{1c}) fasting glucose level, body mass index (BMI)), presence of hypertension and diabetic complications (retinopathy, nephropathy, neuropathy, cardiovascular diseases, cerebrovascular events, extremity pathologies (peripheral vascular diseases and extremity amputation)) of the patients were recorded. In addition, the patients were questioned in terms of dietary compliance, physical exercise, blood glucose monitoring at home and drug compliance in the presence of a dietician. The smoking habits of the patients and the drugs they took were also documented.

Clinical and laboratory measurements

The diagnosis of DM was made according to the American Diabetes Association (ADA) criteria. The systolic and diastolic blood pressures were also measured by employing an automatic blood pressure monitor that had a suitable cuff size on the right hand after a resting period of 10 min. Patients who had systolic/diastolic blood pressure ≥ 140/90 mm Hg or those who were using antihypertensive drugs were evaluated as hypertensive. Height (m) and weight (kg) measurements were made in order to compute the BMI. The BMI was computed by employing the following formula: weight/height × height [13].

Life style and diabetic complications

Accompanied by a dietitian, dieting ≥ 3 days per week, dietary compliance, at least half an hour ≥ 3 days a week were evaluated as *Exercise Compliance*; follow-up of the blood sugar at home ≥ 5 days per week was evaluated as *Blood Glucose Compliance at Home*, not taking medication ≥ 1 per week was evaluated as *Drug Incompatibility*, regular medicine intake was evaluated as *Drug Compliance*. All the patients received eye examination for retinopathy by an eye diseases specialist. In terms of nephropathy, urine analyses were made for protein and creatinine clearance in 24-hour urine. The glomerular filtration rate was computed, and urine ultrasonography was per-

formed. Burns, tingling, pain, stings, etc. in the limbs were questioned orally in the patients; and the presence of neuropathy was also evaluated. In patients who had joint pains, arthropathy was examined by performing direct joint graphs and magnetic resonance imaging. Cardiovascular disease presence was examined by a cardiac and vascular surgeon with examination and electrocardiogram, and by performing echocardiography, coronary angiography and vascular ultrasonography on the patients who necessitated this. The patients were questioned clinically, and the presence of cerebrovascular disease was documented with neurological examination.

Evaluation of smoking

The smoking habits of the participants were questioned in detail. The participants were separated into three groups as *smokers*, *those who had quit smoking* and *non-smokers*. The number of cigarettes consumed by the participants was expressed as package/year (each package has 20 cigarettes). The amount of smoking was computed by multiplying the number of cigarettes smoked and the number of years the participant had smoked. For those who smoked previously, smoking quit times were recorded. Participants who had passive smoking were excluded from the study.

Ethical statement

All participants provided written permission to participate in the present study. Ethical approval was received from the Ethics Committee to conduct this study (Istanbul, Turkey). All the procedures were in line with the Human Experiment Committee, Ethical Standards of our institution and the Helsinki Declaration.

Statistical analysis

The program SPSS 22.0 was used for statistical analysis of the study data. When the variables that were included in the present study were examined in terms of normal distribution, it was determined that the age variable was distributed normally; however, the other variables (diabetic period, waist circumference, BMI and HbA_{1c}) were not distributed normally. The Mann-Whitney *U*-test was used to determine the group which caused the difference; the Kruskal-Wallis test was used to compare the mean values in the data that were not distributed normally; and the ANOVA test was used in analyzing the variables that were distributed normally. Categorical variables were expressed with numbers and percentages, and were analyzed by the χ^2 test. The significance level was taken as $p < 0.05$ in the 95% confidence interval.

Results

A total of 757 type 2 DM patients were included in the present study; 405 (53.5%) of them were female and 352 (46.5%) were male. The age range of the patients was 18–70 years, and the average age was 56.40 ±11.35 years. A total of 54.8% (415 patients) of the patients did not smoke; 12% (91 patients) patients had quit smoking; and 33.2% (251 patients) were still smoking.

When the relation between smoking and demographic, anthropometric characteristics, lifestyle and diabetic complications was examined, it was found that the rate of non-smokers was higher in women, and the percentage of smokers and those who had quit smoking was lower. The rate of non-smokers and quitters was statistically significantly higher in females than in males ($p = 0.001$). While the mean age of non-smokers and quitters was similar, that of smokers was statistically significantly lower compared to non-smokers and quitters ($p = 0.001$). It was observed that HbA_{1c} was statistically significantly higher in smokers and quitters. In this respect, the highest value was detected in smokers and in those who had smoked and quit. While the HbA_{1c} level was statistically significantly higher in smokers than quitters and non-smokers, it was statistically significantly higher in quitters than non-smokers ($p < 0.05$). While no significant differences were detected between the groups in terms of DM duration and BMI, the waist circumference was detected to be statistically significantly higher in smokers and quitters compared to non-smokers ($p < 0.05$) (Table I).

When dietary compliance and smoking were considered, it was observed that there was no significant difference in terms of dietary habits in quitters. It was observed that while smokers did not have dietary compliance at a significantly higher level, dietary compliance was significantly higher in non-smokers ($p < 0.001$). When the relation between exercise and smoking was examined, it was observed that there were no significant differences in terms of doing exercise in the quitters. While the rate of doing no exercise was statistically significantly higher in smokers, the rate of doing exercise was significantly higher in non-smokers ($p < 0.001$). When the blood sugar measurement at home and smoking relation was examined, it was found that there were no significant differences in terms of blood sugar measurement in the quitters. While the rate of blood sugar measurement in smokers was higher, it was observed that the rate of blood sugar measurement was statistically significantly higher in non-smokers ($p < 0.05$). When the relation between drug compliance and smoking was examined, it was found that there were no significant differences

Table I. Relations between smoking, demographic and anthropometric characteristics and diabetic complications

Parameter	Non-smokers	Quitters	Smokers	*P*-value
Gender:				
Female	256 (63.2%)	27 (6.7%)	122 (30.1%)	0.001
Male	159 (45.2%)	64 (18.2%)	129 (36.6%)	
Age [years]	57.70 ±11.53	58.08 ±10.43	53.64 ±10.91	0.001
DM duration [years]	5	5	6	0.254
HbA_{1c} (%)	7	7.8	9	0.001
BMI [kg/m^2]	29	30	30	0.090
Waist circumference [cm]	92	96	96	0.001
Hypertension:				
Yes	284 (51.9%)	71 (13%)	192 (35.1%)	0.034
No	131 (62.4%)	20 (9.5%)	59 (28.1%)	
Dietary compliance:				
Yes	224 (67.3%)	37 (11.1%)	72 (21.6%)	0.001
No	191 (45%)	54 (12.7%)	179 (42.2%)	
Exercise:				
Yes	202 (68%)	34 (11.4%)	61 (20.5%)	0.001
No	213 (46.3%)	57 (12.4%)	190 (41.3%)	
Blood sugar measurement:				
Yes	171 (57.8%)	42 (14.2%)	83 (28%)	0.039
No	244 (52.9%)	49 (10.6%)	168 (36.4%)	
Drug compliance:				
Yes	303 (62.5%)	57 (11.8%)	125 (25.8%)	0.001
No	112 (41.2%)	34 (12.5%)	126 (46.3%)	
Nephropathy:				
Yes	136 (42%)	46 (14.2%)	142 (43.8%)	0.001
No	279 (64.4%)	45 (10.4%)	109 (25.2%)	
Neuropathy:				
Yes	119 (40.9%)	39 (13.4%)	133 (45.7%)	0.001
No	296 (63.5%)	52 (11.2%)	118 (25.3%)	
Retinopathy:				
Yes	133 (40.7%)	40 (12.2%)	154 (47.1%)	0.001
No	282 (65.7%)	51 (11.9%)	96 (22.4%)	
Cerebrovascular:				
Yes	7 (38.9%)	7 (38.9%)	4 (22.2%)	0.002
No	407 (55.1%)	84 (11.4%)	247 (33.5%)	
Cardiovascular:				
Yes	89 (41.4%)	35 (16.3%)	91 (42.3%)	0.001
No	326 (60.1%)	56 (10.3%)	160 (29.5%)	
Arthropathy:				
Yes	12 (36.4%)	5 (15.2%)	16 (48.5%)	0.088
No	403 (55.7%)	86 (11.9%)	235 (32.5%)	
Amputation:				
Yes	3 (50%)	1 (16.7%)	2 (33.3%)	0.935
No	412 (54.9%)	90 (12%)	249 (33.2%)	

DM – diabetes mellitus, BMI – body mass index.

in terms of drug compliance in the quitters. While the rate of drug compliance was statistically significantly higher in smokers, the rate of drug compliance was statistically significantly higher in non-smokers ($p < 0.05$) (Table I).

When the relation between smoking and diabetic complications was examined, it was found that the rate of smoking was higher in hypertension patients than in those who did not have hypertension ($p < 0.05$); and these rates were similar in non-smokers and quitters. In those with nephropathy, while the percentage of non-smokers was statistically significantly lower, the rate of smokers was significantly higher, and no significant differences were detected in quitters ($p = 0.001$). In those with neuropathy, while the percentage of non-smokers was statistically significantly lower, and the rate of smokers was statistically significantly higher, no significant differences were detected in quitters ($p = 0.001$). In those with retinopathy, the rate of non-smokers was statistically significantly lower, the rate of smokers was higher, and no significant differences were detected in quitters ($p = 0.001$). In those with cardiovascular disease, while the rate of non-smokers was statistically significantly lower, and the rate of smokers was statistically significantly higher, no significant difference was found in quitters ($p < 0.05$). There were no statistically significant differences between smoking, arthropathy and amputation values ($p > 0.05$) (Table I).

The patients who had quit smoking were separated into 4 groups according to their quitting periods (< 1-year quitters, 1 ≤ 5-year quitters, 5 ≤ 10-year quitters, > 10-year quitters). Based on the evaluation that was made by taking the group who had never smoked as the reference; the rate of women who were non-smokers and who had quit smoking for less than 1 year was higher than the other groups at a statistically significant level. The average age and diabetes duration mean values were similar between the groups. The HbA_{1c} values of the participants who had quit smoking for more than ten years and who did not smoke were similar, and were lower than the other groups. The BMI values were not different between the groups. The waist circumference values of the non-smokers and the participants who had quit smoking for less than 1 year were statistically significantly lower than other groups. The rate of those who had hypertension was similar among the groups. The dietary compliance was significantly higher in those who did not smoke and those who had quit smoking for more than 10 years. In terms of exercise and blood glucose measurement ratios, there were no significant differences among the groups. However, in groups which had quit smoking for less than 10 years, the rates of doing exercise and blood sugar measurements were lower than in non-smokers; it was observed that the rate of doing exercise and blood sugar measurements were higher than those of non-smokers in those who had quit smoking for more than 10 years. It was also observed that the rate of drug compliance was significantly higher in those who did not smoke and those who had quit smoking for more than 10 years in terms of drug compliance. In terms of nephropathy, the presence of nephropathy was statistically significantly higher in those who had quit smoking for 1–5 years and 5–10 years. The presence of neuropathy was significantly more frequent in those who had quit smoking for 5–10 years compared to the others. The presence of retinopathy was statistically significantly less frequent in those who had quit smoking for over 10 years. The presence of cerebrovascular disease was statistically significantly higher in those who had quit smoking for 1–5 years than the others. The presence of cardiovascular disease was statistically significantly less frequent in the non-smokers than in the other groups ($p < 0.05$). When the groups were evaluated in terms of the relevant complications, it was observed that the complication rates were lower in those who had quit smoking for more than 10 years than other groups, and that the complication rate approached the values of the non-smoking group. There were no differences between the groups in terms of the rate of patients with arthropathy ($p > 0.05$) (Table II).

Discussion

Accelerated atherosclerosis is the most important factor in the development of macrovascular complications in diabetic patients. Dyslipidemia, dysinsulinemia, increase in oxidative stress, increase in platelet activation, inflammation, activation of the renin-angiotensin-aldosterone system, and increased endothelin 1 levels result in endothelial dysfunction, which eventually leads to a tendency to thrombosis. Together with the accelerated atherosclerosis, this causes the formation of macrovascular complications due to diffuse vascular involvement. Again, similarly, microvascular complications such as retinopathy, neuropathy and nephropathy develop in the same way with the disruption of the microvascular circulation [14]. In addition, it was shown in previous studies that there is a relation between smoking and diabetic development, bad glycemic control and diabetic complications [10–12]. Since chronic cigarette smoking causes an inadequate compensatory insulin response, it is meanwhile a high risk factor for insulin resistance leading to the development of insulin resistance syndrome and type 2 DM [10, 11]. In previous studies, it was found that the risk was 61% for heavy smokers (at least 20 cig-

Table II. Relations between quitting smoking, demographic and anthropometric characteristics and diabetic complications

Parameter	Non-smokers	< 1 year quitters	1 ≤ 5 year quitters	5 ≤ 10 year quitters	> 10 year quitters	*P*-value
Gender:						
Female	256 (61.7%)	6 (54.5%)	5 (17.9%)	8 (27.6%)	8 (34.8%)	0.001
Male	159 (38.3%)	5 (45.5%)	23 (82.1%)	21 (72.4%)	15 (65.2%)	
Age [years]	57.7 ±11.53	54.36 ±7.87	55.25 ±10.84	58.83 ±10.17	62.35 ±10.22	0.171
DM duration [years]	5	5	6	5	5	0.941
HbA_{1c} (%)	7	8	7.9	7.7	6.9	0.016
BMI [kg/m^2]	29	28	30	30	31	0.240
Waist circumference [cm]	92	92	96.5	98	96	0.005
Hypertension:						
Yes	284 (68.4%)	9 (81.8%)	20 (71.4%)	22 (75.9%)	20 (87%)	0.300
No	131 (31.6%)	2 (18.2%)	8 (28.6%)	7 (24.1%)	3 (13%)	
Dietary compliance:						
Yes	224 (54%)	3 (27.3%)	9 (32.1%)	11 (37.9%)	14 (60.9%)	0.030
No	191 (46%)	8 (72.7%)	19 (67.9%)	18 (62.1%)	9 (39.1%)	
Exercise:						
Yes	202 (48.7%)	4 (36.4%)	7 (25%)	10 (34.5%)	13 (56.5%)	0.060
No	213 (51.3%)	7 (63.6%)	21 (75%)	19 (65.5%)	10 (43.5%)	
BS measurement:						
Yes	171 (41.2%)	4 (36.4%)	15 (53.6%)	9 (31%)	14 (60.9%)	0.161
No	244 (58.8%)	7 (63.6%)	13 (46.4%)	20 (69%)	9 (39.1%)	
Drug compliance:						
Yes	303 (73%)	6 (54.5%)	15 (53.6%)	16 (55.2%)	20 (87%)	0.012
No	112 (27%)	5 (45.5%)	13 (46.4%)	3 (44.8%)	3 (13%)	
Nephropathy:						
Yes	136 (32.8%)	3 (27.3%)	15 (53.6%)	17 (58.6%)	11 (47.8%)	0.008
No	279 (67.2%)	8 (72.7%)	13 (46.4%)	12 (41.4%)	12 (52.2%)	
Neuropathy:						
Yes	119 (28.7%)	5 (45.5%)	10 (35.7%)	16 (55.2%)	8 (34.8%)	0.034
No	296 (71.3%)	6 (54.5%)	18 (64.3%)	13 (44.8%)	15 (65.2%)	
Retinopathy:						
Yes	133 (32%)	4 (36.4%)	15 (53.6%)	15 (51.7%)	6 (26.1%)	0.038
No	282 (68%)	7 (63.6%)	13 (46.4%)	14 (48.3%)	17 (73.9%)	
CVE:						
Yes	7 (1.7%)	1 (9.1%)	3 (10.7%)	2 (6.9%)	1 (4.3%)	0.017
No	407 (98.3%)	10 (90.9%)	25 (89.3%)	27 (93.1%)	22 (95.7%)	
CVD:						
Yes	89 (21.4%)	4 (36.4%)	9 (32.1%)	14 (48.3%)	8 (34.8%)	0.007
No	326 (78.6%)	7 (63.6%)	19 (67.9%)	15 (51.7%)	15 (65.2%)	
Arthropathy:						
Yes	12 (2.9%)	1 (9.1%)	0 (0%)	1 (3.4%)	3 (13%)	0.067
No	403 (97.1%)	10 (90.9%)	28 (100%)	28 (96.6%)	20 (87%)	

DM – diabetes mellitus, BMI – body mass index, BS – blood sugar, CVE – cerebrovascular events, CVD – cardiovascular diseases.

arettes a day), 29% for less heavy smokers (less than 20 cigarettes a day) and 23% for old smokers [10, 11].

Exposure to nicotine causes β-cell dysfunction, increases in β-cell apoptosis and decreases in beta-cell volume [15]. The apoptosis induced by nicotine leads to dysglycemia and obesity. In addition, the mitochondrial dysfunction, which is caused by nicotine, induces oxidative stress and inflammatory apoptosis, and causes losses in pancreas beta cells. This is related to less insulin release [15, 16]. In empirical and clinical studies, it was shown that cigarette smoking reduces insulin sensitivity and results in glucose and lipid metabolism disorders such as dyslipidemia and hyperglycemia [12]. In diabetic patients, smoking makes metabolic control difficult, and requires higher doses of insulin to have the same metabolic targets as in non-smokers [12]. It is also already known that smoking increases the blood glucose levels by increasing the counter-regulatory hormones such as catecholamines and corticosteroids. When the close relation between diabetic complications and hyperglycemia is considered, it is observed that smoking is an important risk factor for the development of diabetic complications [10, 11].

In the study that was conducted in 2012 by Chakkarwar, it was reported that smoking is an independent risk factor for the development and progression of diabetic nephropathy, and there is a strong relation between smoking and diabetic microvascular complications. Smoking and hyperglycemia cause TGF-β upregulation and glycation end-product accumulation because they increase oxidative stress and lipid accumulation. It was also reported that by reducing nitric oxide production, it causes the formation of nephropathy as a result of the thinning of the glomerular basement membrane and by leading to glomerulosclerosis and interstitial fibrosis [17]. Goetz *et al.* conducted a study in 1997 on 455 people, and found that the rate of the decrease in creatinine clearance levels was higher in time in participants who still smoked and who had quit smoking than in those who did not smoke [18]. In our study, we too detected an increase in the diabetic nephropathy risk with smoking, which is similar to the results of the above-mentioned studies.

Diabetic retinopathy is a global health problem which occurs with microaneurysm, macular edema, and neovascularization, and may result in blindness. It was determined that neuronal cell loss occurred with early stage visual dysfunction [19]. In addition, in previous studies, a relation was found between diabetic retinopathy and major clinical illnesses such as stroke, coronary heart disease, heart failure, and renal failure [19]. Boretsky *et al.* conducted a study in 2015 on rats with experimentally induced diabetes. These rats were exposed to nicotine. They observed damage to the retina and concluded that this might lead to diabetic retinopathy progression [20]. Hu *et al.* conducted a study in 2005, and found that smoking caused an increase in total homocysteine levels in patients who had grade 2 diabetic retinopathy, and claimed that this could be an independent and facilitating factor for arteriolar retinopathy [21]. In our study, too, the rate of diabetic retinopathy was statistically significantly higher in smoking patients than in non-smoking patients. Diabetic neuropathy is one of the most common chronic complications, and is also the most important cause of morbidity. Clair *et al*. conducted a meta-analysis and included 38 studies between 1996 and 2014, and reported that there might be a relation between smoking and diabetic neuropathy [22]. Similarly, Mitchell *et al.* conducted another study and detected a significant relation between smoking and diabetic neuropathy [23]. Similar results were obtained in our study, and it was observed that neuropathy occurred more frequently in smoking diabetic patients.

Previous studies have shown that diabetes and smoking are two independent and changeable risk factors for cerebrovascular disease development. In a study conducted by Phipps *et al.*, they found that the risk of stroke increased at least two-fold in diabetic patients compared with non-diabetic patients, and reported that the symptoms developed earlier and were more severe [24]. In our study, we found similar results as in the above-mentioned studies. We especially concluded that as smoking increased, the number of cerebrovascular diseases also increased, and as years passed after quitting smoking, this risk decreased gradually in time. Cardiovascular diseases are the leading cause of mortality throughout the world, and are reported to account for 70% of deaths due to all chronic diseases. Diabetes mellitus may mainly cause heart failure, myocardial infarction, angina pectoris, and arrhythmia [25]. In the present study, we detected a statistically significant increase in cardiovascular diseases in diabetic patients who smoked. Since the rate of smoking was higher in patients who had hypertension, it is considered to play a role in the increase of cerebrovascular and cardiovascular diseases. In our study, it was observed that the occurrence of complications was lower in those who had quit smoking for more than 10 years than in the other groups, and that the rate of occurrence of complications was close to that of the non-smoker group.

As a result, we concluded in our study that there were statistically significant increases with smoking in the complications of type 2 DM in patients who had bad lifestyles. In diabetic patients, smoking is the most important and changeable risk factor. Smoking was found to be related to earlier

development and progression of macrovascular and microvascular complications. Due to the difficulty in patient compliance with pharmacological treatments, and the progressive decrease in the β-cell reserves, which occur when the diabetes duration lasts for longer durations, nonpharmacologic therapy often becomes compulsory to provide optimal glycemic control. All the members of the diabetes team (doctors, nurses, dieticians, and psychologists) should always advise their diabetic patients to quit smoking with every opportunity and in a persistent manner, question the amount of cigarettes being smoked per day and how long they have smoked, support their patients who are at risk of restarting smoking, and include routine diabetes care/smoking quitting methods whose effectiveness has been proven.

Conflict of interest

The authors declare no conflict of interest.

References

1. Satman I, Imamoglu S, Yılmaz C, Akalın S ve Diabetes Mellitus Study and Training Group. TEMD Diabetes Mellitus and it's Complications Diagnosis, Treatment and Monitoring Guide, 5. Printing. Bayt Typography, Ankara, 2011.
2. Hilton DJ, OÕRourke PK, Welborn TA, Reid CM. Diabetes detection in Australian general practise: a comparison of diagnostic criteria. Med J Aust 2002; 176: 104-7.
3. da Rocha Fernandes J, Ogurtsova K, Linnenkamp U, et al. IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. Diabetes Res Clin Pract 2016; 117: 48-54.
4. The TURDEP Group. Population-Based Study of Diabetes and Risk Characteristics in Turkey. Diabetes Care 2002; 25: 1551-6.
5. Satman I; the TURDEP Group. Population-Based Study of Diabetes and Risk Characteristics in Turkey. 32. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi özet kitabı,13-17 Ekim 2010, Antalya, 2010; 24-9.
6. Menzin J, Langley-Hawthor C, Friedman M, Boulanger L, Cavanaugh R. Potential short-term economic benefits of improved glycemic control: a managed care perspective. Diabetes Care 2001; 24: 51-5.
7. International Expert Committee. International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes. Diabetes Care 2009; 32: 1327-34.
8. WHO Report on the Global Tobacco Epidemic, MPOWER, WHO, 2008.
9. Global Adult Tobacco Survey, Turkey Report, Ministry of Health, Publ. 2 July 2010.
10. Carlsson S, Midthjell K, Grill V. Smoking is associated with an increased risk of type 2 diabetes but a decreased risk of autoimmune diabetes in adults: an 11-year follow-up of incidence of diabetes in the Nord-Trondelag study. Diabetologia 2004; 47: 1953-6.
11. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA 2007; 298: 2654-64.
12. Smith U, Axelsen M, Carvalho E, Eliasson B, Jansson PA, Wesslau C. Insulin signaling and action in fat cells: associations with insulin resistance and type 2 diabetes. Ann N Y Acad Sci 1999; 892: 119-26.
13. American Diabetes Association. Standards of Medical Care in Diabetes. Diabetes Care 2015; 38: 8-67.
14. Summary of Revisions for the 2009 Clinical Practice Recommendations. Diabetes Care 2009; 32: 754.
15. Yoshikawa H, Hellstrom-Lindahl E, Grill V. Evidence for functional nicotinic receptors on pancreatic beta cells. Metabolism 2005; 54: 247-54.
16. Bruin JE, Gerstein HC, Morrison KM, Holloway AC. Increased pancreatic beta-cell apoptosis following fetal and neonatal exposure to nicotine is mediated via the mitochondria. Toxicol Sci 2008; 103: 362-70.
17. Chakkarwar VA. Smoking in diabetic nephropathy: sparks in the fuel tank?. World J Diabetes 2012; 3: 186-95.
18. Halimi JM, Giraudeau B, Vol S, et al. Effects of current smoking and smoking discontinuation on renal function and proteinuria in the general population. Kidney Int 2000; 58: 1285-92.
19. Zheng Y, He M, Congdon N. The worldwide epidemic of diabetic retinopathy. Indian J Ophthalmol 2012; 60: 428-31.
20. Boretsky A, Gupta P, Tirgan N, et al. Nicotine accelerates diabetes-induced retinal changes. Curr Eye Res 2015; 40: 368-77.
21. Hu R, Zhang XX, Wang WQ, Lau CP, Tse HF. Smoking, homocysteine and degree of arteriolar retinopathy. Atherosclerosis 2005; 183: 95-100.
22. Clair C, Cohen MJ, Eichler F, Selby KJ, Rigotti NA. The effect of cigarette smoking on diabetic peripheral neuropathy: a systematic review and meta-analysis. J Gen Intern Med 2015; 30: 1193-203.
23. Mitchell BD, Hawthorne VM, Vinik AI. Cigarette smoking and neuropathy in diabetic patients. Diabetes Care 1990; 13: 434-7.
24. Phipps MS, Jastreboff AM, Furie K, Kernan WN. The diagnosis and management of cerebrovascular disease in diabetes. Curr Diab Rep 2012; 12: 314-23.
25. Yusuf S, Reddy S, Ôunpuu S, Anand S. Global burden of cardiovascular diseases: part i: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001; 104: 2746-53.