

Original Research / ÖzgünAraştırma

Does a High Pre-Treatment Nicotine Dependence Increase the Post-Cessation Diabetes Risk?

Tedavi Öncesi Yüksek Nikotin Bağımlılığı Sigarayı Bırakma Sonrası Diyabet Riskini Artırır mı?

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ABSTRACT

Aim:This study aimed to observe the pre-treatment nicotine dependence level (NDL) and the change in diabetes risk screening results during the post-cessation period. **Material and Methods:** In the current study, 527 current smokers who applied to a tertiary hospital for smoking cessation treatment between February 2019 and July 2019 were included. Firstly, a questionnaire (containing demographic data, the Fagerstrom Nicotine Dependence Test; FTND, and the American Diabetes Association; ADA Diabetes Risk Screening Tool) was applied. In the second stage, smoking cessation status and diabetes risk of 279 patients who could be reached by phone after 6 months were re-evaluated. **Results:**Based on initial results, 33.6% of nicotine addicts were heavy smokers and 20.5% had type 2 diabetes mellitus (T2DM) risk. Although FNBT score and diabetes risk score (p = 0.002, r = 0.133) were related, NDL was not effective in the presence of T2DM risk before quitting (p = 0.08). Increased post-cessation T2DM risk was detected in quitters (25.3%) versus current smokers (13.5%).Six-month follow-up indicated that the rate of diabetes risk among current smokers was 46% of quitters (p=0.01, OR=0.46;0.25-0.86). The diabetes risk presence related to pre-treatment heavy dependence among quitters (54.1%) was higher than mild (13.5%) or moderate (32.4%) nicotine dependence (p=0.004). Although final BMI was not different between quitters and smokers (p=0.58), there was a significant increase in BMI between baseline and final visits (p<0.001; Z=-10.39). Both current smokers and quitters had similar age and gender demographics (p=0.64, p=0.37, respectively). **Conclusion**:Particularly heavy smokers might be aware that smoking cessation would be more rational with a lifestyle change to prevent diabetes risk of the post-cessation period. Our study would contribute to knowledge about smoking, post-cessation, and T2DM risk.

Key words: Diabetes risk test, public health, smoking, type 2 diabetes

ÖZET

Amaç: Bu çalışma, tedavi öncesi nikotin bağımlılık düzeyini (NBD) ve sigara bırakma tedavisi sonrası diyabet risk tarama sonuçlarındaki değişimi gözlemlemeyi amaçlamıştır. Gereç ve Yöntemler: Şubat 2019 ile Temmuz 2019 tarihleri arasında sigara bırakma tedavisi için üçüncü basamak bir hastaneye başvuran toplam 527 sigara kullanan gönüllü bu çalışmaya dahil edilmiştir. Önce demografik veriler, Fagerstrom Nikotin Bağımlılığı Testi (FNBT) ve diyabet riskinin taranmasına yönelik Amerikan Diyabet Derneği (ADA) Diyabet Risk Test'ini içeren soru formu katılımcılara uygulanmıştır. 6 ay sonra telefonla ulaşılabilen 279 katılımcının sigara bırakma durumları ve diyabet riskleri veniden değerlendirilmiştir. Bulgular: Çalışmanın başlangıcında, sigara içenlerin %33,6'sı ağır düzeyde sigara bağımlısı olup, %20,5'inde tip 2 diyabetesmellitus (T2DM) riski saptanmıştır. FNBT skoru ve diyabet risk skoru (p=0,002; r=0,133) ilişkili olsa da, NBD bırakma öncesi T2DM risk varlığında etkili olmamıştır (p=0,08). Tedavi sonrası sigarayı bırakanların (% 25,3) sigara içmeye devam edenlere (% 13,5) göre T2DM riskinin arttigi tespit edilmiştir. Altı aylık takip, sigaraya devam edenlerde diyabet risk oranının sigarayı bırakanların % 46'sı kadar (p = 0,01 OR = 0,46; 0,25-0,86) olduğunu göstermiştir. Sigarayı bırakanlar arasında diyabet riski ile ilişkili tedavi öncesi ağır bağımlılık (% 54,1), hafif (% 13,5) veya orta (% 32,4) bağımlılıktan daha fazla oranda izlenmiştir (p = 0,004). Tedavi öncesi ve sonrası vücut kitle indeksinde (VKİ) anlamlı bir artış olsa da (p <0,001; Z = -10,39), tedavi sonrası sigarayı bırakanlar ile içmeye devam edenlerin VKİ değerleri arasında fark bulunmamıştır (p: 0,58). Hem sigara içenlerin hem de bırakanların benzer yaş ve cinsiyet özelliklerine sahip olduğu görülmüştür (sırasıyla p = 0,64, p = 0,37). Sonuç: Özellikle ağır düzeyde sigara bağımlılığı olanlar, bırakma sonrası dönemde diyabet riskini önlemek için yaşam tarzı değişikliği ile beraber sigara bırakmanın daha akılcı olacağının farkında olmalıdır. Çalışmamız sigara bağımlılığı, sigara bırakma sonrası dönem ve T2DM riski hakkında literature katkı sağlayacaktır.

Anahtar kelimeler: Diyabet risk testi, halksağlığı, sigara, tip 2 diyabet

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INTRODUCTION

The global prevalence of tobacco use in type 2 diabetes (T2DM) is 20.81%.¹ Increased risk of T2DM is associated with active smoking.² A linear dose-response relationship between cigarette consumption and T2DM risk has been reported.³ To emphasize the importance of smoking cessation in T2DM, a section on tobacco use and cessation was added to the revisions of the Standards of Medical Care in Diabetes published in 2019 by the American Diabetes Association (ADA).⁴

Potential mechanisms of nicotine-induced insulin resistance have been explained in various ways. Adiponectin levels that fall with smoking and rise with smoking cessation, but may also fall with smoking cessation in the presence of post-cessation weight gain.⁵ Consistent with the adverse effects of nicotine on insulin sensitivity, there is a clear, dosedependent relation between diabetes or glucose intolerance and both active and passive cigarette exposure.6A relative risk reduction of 40%-70% in adults with prediabetes is possible with lifestyle interventions like smoking cessation and weight loss.7 A minimum of 3-year follow-up seemed to be required to display a reduction in diabetes risk in highrisk individuals.⁸The use of validated risk calculators to quickly identify and, follow-up people at a high risk of T2DM is recommended by several international organizations.9 The ADA Diabetes Risk test was chosen in this study because the test is a simple, fast, and noninvasive screening tool to identify individuals at high risk for diabetes.

To our knowledge, our study is a novel study exploring the relationship between diabetes risk screening tools and smoking before and after smoking cessation. We aimed (i) to compare diabetes risk and related factors of smokers at the beginning of treatment; and (ii) to evaluate the effect of a six-month post-cessation period on the T2DM risk score between quitters and current smokers.

MATERIALS AND METHODS

Study design, sample, and procedures

Study data were collected from 527 smokers who applied to smoking-cessation treatments of family medicine clinics at a tertiary hospital between February 2019 and July 2019. In the first step, patients were asked to fill out a questionnaire including demographic data, the Fagerstrom Test for Nicotine Dependence (FTND), and the American Diabetes Association (ADA) Diabetes Risk Test. The second step was six months later; 279 of 527 patients were reached by phone and answered the control questionnaire containing control T2DM risk score and cessation success (quit or continue smoking). Patients of the second stage were grouped into current smokers or quitters. The other participants who might not be reached or refused to reply to questions were excluded from the second stage. Participants with a prior DM diagnosis or with a disease or drug use history that may cause DM were not included.

The ADA Diabetes Risk Test contains seven questions about age, gender, presence of gestational diabetes diagnosis, presence of hypertension diagnosis, family history of diabetes, weight, and physical activity status. The tool is used to determine who should be assessed for diabetes risk in asymptomatic adults. Patients scoring 5 or higher are at risk of having T2DM, according to the diabetes risk test and these patients should be seen by a health professional for T2DM diagnoses.¹⁰Patients with prediabetes are defined by the American Diabetes Association as a fasting plasma glucose of 100-125 mg/dL or 2-h plasma glucose value during a 75-g oral glucose tolerance test of 140-199 mg/dL or hemoglobin A1c (HbA1c) levels of 5.7%-6.4%.¹⁰

Reliability in the Turkish version of FTND and factor analysis was done in 2004 by Uysal et al.¹¹ Smoking was classified with FTND score in mild (0–4 points), moderate (5–7 points), and heavy (8–10 points) dependence severity as in some studies using 3 levels instead of 5 levels.¹²

Statistical analysis

Categorical data were compared using Chi-square tests. Continuous data were analyzed by Mann– Whitney U and Spearman correlation tests. Changes in T2DM risk scores and BMI were compared using the Wilcoxon test. Data were analyzed using NCSS 10 (2015 Kaysville, USA). A p-value of 0.05 was considered statistically significant.

Compliance with ethical standards

The participants were informed about the survey and, consequently, the verbal consent of patients was obtained. Only volunteers were included in the study. The Taksim Ethics Committee reviewed and approved this study on 16/01/2019 (Approval no:14). All authors read and comply with the principles of the Helsinki Declaration. This article does not contain any studies with animals.

RESULTS

Evaluation of demographic data, addiction, and pre-treatmentdiabetes risk

Patients (n=527; age=40.1±11.46) who applied for smoking cessation treatment were enrolled in the first

step of this study. Males were 60.2% of the cases and 33.6% were heavy smokers. The duration time of smoking was 22.1±11.8 years. Daily cigarette consumption was 25.27±12.94 cigarettes/per day, and lifetime cigarette consumption was 28.49±22.63 packs/year. Pre-treatment BMI was 26.5±4.6 kg/m2. Fasting blood glucose (FBG) was 82.7±14.8 mg/dl and 10.4% of all patients had a FBG between 100 and 125 mg/dl, indicating the presence of Prediabetes. The pre-treatment diabetes risk score of participants was 3.10±1.78 and 20.5% of the patients were classified as positive diabetes risk, defined as risk score ≥ 5 points. At the same time, smokers with prediabetes had a significantly higher (p=0.01)daily cigarette consumption $(30\pm16.5 \text{ cigarettes per/day})$ than smokers without Prediabetes (25±12.4 cigarettes per/day). The diabetes risk score in men was higher than that of women (female score: 2.97±02.05, male score: 3.18±1.58) but gender frequency was not different for T2DM risk presence.

As shown in **Table 1**, patients were categorized based on initial diabetes risk scores. Age (p<0.001), FBG (p<0.001), education (p<0.001), BMI (p<0.001), FTND score (p=0.04), duration of smoking

(p<0.001), mean daily consumption of cigarettes (p=0.02) and presence of any cardio vascular system / respiratory system (CVS/RS) disease (<0.001) were significantly higher in those at risk for DM compared with those not at risk.

Comparison of nicotine dependence groups

In **Table 2**, patients were categorized into mild, moderate, or heavy NDL groups. Heavy smokers were older (p=0.03), had a longer duration of smoking (p=0.02), a higher daily cigarette consumption (p<0.001), a higher lifetime cigarette consumption (p<0.001), and a higher BMI (p<0.001) compared with the mild or moderate smokers. Diabetes risk was not significantly different between the nicotine dependence groups (p=0.08).

A weak correlation was found between FTND score and diabetes risk score (p=0.002, r=0.133) using a Spearman test.

Test groups	Age (year)	Gender		Education		CVS/RS disease		Fasting Blood Glucos	BMI	FTND Score	Daily cigarette consumpti	Duration of smoking
		Female	Male	Illiterate/ Basic education	High school/ Univer sity	(-)	(+)	e			on (per day)	(years)
	Mean ±SD	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD
DM	37.1±	163	256	191	228	345	74	79.99±	24.54±	6.3±	24.4±	19.4±
Risk (–)	9.92	(77.6%)	(80.8%)	(68.7%)	(91.6%)	(90.6 %)	(50.7%)	14.21	4.11	2.14	11.70	10.21
DM	51.7±	47	61	87	21	36	72	93.20±	30.21±	6.70±	$28.5 \pm$	32.7±
Risk (+)	9.53	(22.4%)	(19.2%)	(31.3%)	(8.4%)	(9.6 %)	(49.3%)	18.86	4.55	2.36	16.56	11.58
P	<0.001*	0.38*	*	<0.001**	•	< 0.001	**	<0.001 *	<0.001*	0.04*	0.02*	< 0.001*

Table 1. Evaluation of patient characteristics in diabetes risk groups at the first step of the study.

Table 2. Evaluation of demographic data according to nicotine dependence severity.

Variables	Mild	Moderate NDL	Heavy	Total score	P-Value
	NDL		NDL		
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Continuous variables					
Age (years)	40.4±11.82	40±11.79	41.7±10.62	40.1±11.46	0.03*
Duration of smoking (years)	21.7±12.66	20.98±11.75	23.91±11.15	22.10±11.78	0.02*
Daily cigarette consumption	15.81±8.12	23.49±8.64	33.16±15.45	25.27±12.94	< 0.001*
(cig per day)					
Lifetime cigarette	17.02±13.54	25.17±17.99	39.7±27.43	28.49±22.63	< 0.001*
consumption (packs/year)					
BMI (kg/m ²)	25.71±4.13	25.98±4.39	27.67±4.93	26.50±4.60	< 0.001*
Categorical variables					

Groups		Mild NDL	Moderate NDL	Heavy NDL	Total	P-Value	
		n (%)	n (%)	n (%)	n (%)		
Gender	Female	40 (7.6%)	91 (17.2%)	79 (15%)	210 (39.8%)	0.24	
	Male	61 (11.6%)	158 (30%)	98 (18.6)	317 (60.2)		
Education	Illiterate	3 (0.6%)	6 (1.1%)	8 (1.5%)	17 (3.2%)	0.91	
	Basic education	49 (9.3%)	122 (23.1%)	90 (17.1%)	261 (49.5%)	-	
	High school	33 (6.3%)	83 (15.7%)	55 (10.4%)	171 (32.4%)		
	University	16 (3%)	38 (7.2%)	24 (4.6%)	78 (14.8%)		
	No	67 (17.6%)	194 (36.8%)	120 (22.8%)	381 (72.3%)		
Diabetes Risk test (ADA)	<5 points (-) risk	82 (15.5%)	206 (39.1%)	131 (24.9%)	419 (79.5%)	0.08	
	\geq 5 points (+) risk	19 (3.6%)	43 (8.2%)	46 (8.7%)	108 (20.5%)		

Table 3. Logistic regression analysis results for diabetes risk and related factors.

Criteria	Risk Factors	P-Value	OR (RR)	95% CI		Predicted-Observed (Percentage correct)
Diabetes Risk	Age*	< 0.001*	1.13	1.08	1.19	87.3%
	Education (High	0.30	0.69	0.34	1.40	
	school/University)					
	FBG (Fasting Blood	0.01*	1.03	1.01	1.05	
	Glucose)*					
	FTND score	0.13	0.76	0.53	1.09	
	Duration of smoking (year)	0.77	0.99	0.93	1.05	
	Daily time cigarette (per	0.77	0.98	0.94	1.05	
	day)					
	Lifetime cigarette (packet/year)	0.36	1.02	0.98	1.06	
	NDL (Heavy)	0.16	0.20	0.02	1.94	
	Presence of CVS/RS	< 0.001*	3.77	2.06	6.92	7
	diseases*					
	BMI *	< 0.001*	1.25	1.15	1.35	

Table 3 depicts the logistic regression analysis results to determine the risk factors in those with diabetes risk. Smokers with diabetes risk had 13% older age, 25% higher BMI, 0.03% higher FBG, and approximately four times more CVS / RS disease presence than those without diabetes risk. Fagerstrom score, dependence severity, and consumption of cigarettes were not risk factors for diabetes risk screening among smokers.

Follow-up assessment of study sample

In the second stage of the study, 279 of 527participants could be reached by phone in the sixth-month of cessation treatment. Smoking cessation success and 2^{nd} diabetes risk test were questioned. Of the participants, 52% (146/279) cases were successful after treatment. Quitters and current smokers were evaluated based on (i) 1strisk scores at the beginning

of the study and (ii) final risk scores in the 6-month follow-up phone interview. While the1stdiabetes risk score was 3.20 ± 1.20 with an 18.3% (51/279) rate, the final diabetes risk score was 3.29 ± 1.65 witha 19.7% (55/279) rate. The Wilcoxon test also showed that the 1stand final diabetes risk scores were significantly different(p<0.001;Z=-5.00) in the second stage.

Despite, no difference in final diabetes risk scores was detected between quitters and current smokers (p=0.23), there was an increase in the diabetes risk score from baseline to final evaluation. As shown in Table 4, quitters had a higher ratio for diabetes risk (37/109) than that of current smokers (18/115). Odds ratio calculation has shown that the presence of diabetes risk rate among current smokers was 46% of quitters (p=0.01 OR=0.46;0.25-0.86). The baseline and final BMI of the study sample in the second stage were 26.63 ± 4.41 and 27.17 ± 4.50 kg/m², respectively. Although there were no differences in the final BMI between quitters and current smokers (p=0,58), there was a significant increase in BMI between 1st and final controls (p<0.001; Z=-10.39). Age and gender

differences were not found between quitters and continuing smokers (p=0.64, p=0.37, respectively).

and moderate dependence (p=0.004) (Table 5). It has seemed that this increased risk cause of quitters.

The diabetes risk related to heavy dependence had a significant increase more than mild

Groups		Quitters (n=146)	Current Smokers (n=133)	Р
		Mean±SD (n%)	Mean±SD (n%)	
Diabetes Risk Test score	First	3.28±1.75	3.09±1.46	0.33**
	Final	3.42±1.78	3.14±1.47	0.23**
Diabetes Risk Group	≥5 points (risk+)	37 (25.3%)	18 (13.5%)	0.01*
-	<5 points (risk-)	109 (74.7%)	115 (86.5%)	
Age	Final	39.05±12.18	37.92±9.69	0.64**
Gender	Male	128 (87.7%)	121 (91%)	0.37*
	Female	18 (12.3%)	12 (9%)	
BMI	Final	27.30±4.78	27.01±4.20	0.58**

Table 4. Evaluation of post-smoking cessation T2DM risk, BMI and gender between quitters and current smokers

Table 5. Evaluation of post-cessation T2DM risk based on pre-treatment NDL of quitters

Final Diabetes Risk Screening		First NDL	First NDL	First NDL	Total	P-Value
		Mild, n (%)	Moderate, n (%)	Heavy n (%)	n (%)	
Quitters	Risk (-)	23 (21.1%)	60 (55%)	26 (23.9%)	109 (100%)	0.004*
	Risk (+)	5 (13.5%)	12 (32.4%)	20 (54.1%)	37 (100%)	
Current	Risk (-)	18 (15.7%)	58 (50.4%)	39 (33.9%)	115 (100%)	0.28*
Smokers	Risk (+)	1 (5.3%)	8 (44.4%)	9 (50%)	133 (100%)	
Total	Risk (-)	41 (18.3%)	118 (52.7%)	65 (29%)	224 (100%)	0.004*
	Risk (+)	6 (11%)	20 (36.3%)	29 (52.7%)	55	
					(100%)	
*Chi-Square 1	test P-value<0.05 signific	cant	· · · ·	•		•

DISCUSSION

Our study found out that increased T2DM risk among quitters in an early period of post-cessation might be related to heavy NDL before treatment. Although pre-treatment T2DM risk was similar in all smokers, the final T2DM risk rate in smokers was 46% of quitters.

Smoking and T2DM

A large cohort study demonstrated a doseresponse relationship between smoking and the incidence of diabetes.¹³ In a Japanese meta-analysis, T2DM risk remained high among quitters during the preceding 5 years. However, there was no risk difference between smokers and non-smokers, and 6.9% of smokers had a high diabetes risk in another study. ¹⁴ An Indonesian study showed that the elders who smoke 1–12 cigarettes per day, 13–24 cigarettes per day, and more than 24 cigarettes per day have risks of 1.3, 1.6, and 2.5 (95% CI, 1.54–3.97), respectively, to get chronic complications compared with those who do not smoke.¹⁵ In our study, nicotine dependence levels (mild, moderate, or heavy smoking) were not statistically different between diabetes risk positive and negative groups before cessation treatment, although FTND scores were higher in the diabetes risk positive group. We did not detect a significant limit of daily cigarette consumption despite a significant correlation between daily consumption (per day) and T2DM risk.

Change in Diabetes Risk Test Scores with Post-Cessation

In an analysis setting the long-term risk of postcessation, the highest diabetes risk occurred in the first 3 years, and then gradually decreased to 0 at 12 years. Compared with adults who never smoked, the hazard ratios of diabetes among former smokers, new quitters, and current smokers were 1.22 (CI, 0.99 to 1.50), 1.73 (CI, 1.19 to 2.53), and 1.31 (CI, 1.04 to 1.65), respectively.¹⁶ Weight gain after smoking cessation attenuates the reduction in risk of developing cardiovascular disease but does not attenuate the beneficial effect of smoking cessation on mortality. These findings confirm the overall health benefits of smoking cessation among people with type 2 diabetes, but also emphasize the importance of weight management after smoking cessation to maximize the health benefits.¹⁷

We found that the smoking cessation period affected diabetes risk development in the first six months based on T2DM risk screening tool results. In a study about post-cessation weight gain, long term increases in weight and BMI occurred in quitters completely or for a while.¹⁸ According to a study conducted in 2013, daily cigarette consumption and FTND levels were strongly associated with BMI increases after smoking cessation; weight gain was higher in participants with FTND scores of 8 points and above compared to participants with FTND scores of 7 or below.¹⁹ In our study, there was a difference in the first BMI measures between the NDL groups; heavy smokers had a higher BMI. Although a significant overall BMI increase occurred, no difference in final BMI between current smokers and quitters was obtained. We speculated that the increased risk of T2DM might be related to weight gain after smoking cessation. The ADA Risk Test questions do not clearly evaluate the patient's selfactivity; therefore, future studies should focus on weight gain versus activity level for T2DM risk in the post-cessation period.

Diabetes Risk Test and T2DM

A study among university students and employees indicated that 37.5% of students and 61.1% of employees had diabetes risk based on the diabetes risk test. Of the study participants, 14.0% of the students and 31.8% of the employees were smokers. The study suggested that diabetes risk was considerable in the young population and advised changing lifestyles to improve diabetes risk.²⁰ The overall prevalence of prediabetes was 25.3% in the population according to an analysis of the 2015 health, well-being, and aging study based on the ADA. In the Jackson Heart Study,18% of participants had prediabetes and 12.7% of participants were current smokers²¹. In our study, the presence of prediabetes determined by FBG was 10.4% and all participants were current smokers at baseline. Ethnicity and smoking rate in research might account for the differences between the studies.

The International Diabetes Federation (IDF) recommends a two-step approach in which diabetes risk be determined first using the risk questionnaire forms, followed by determination of blood glucose levels in people at risk for diabetes.²² A novel review found out that interventions should be targeted at people at risk to improve recruiting and intervention effectiveness. Screening questionnaires and blood glucose measurement can both be used for screening; the method does not appear to affect intervention effectiveness. Screening and recruitment are timeconsuming, targeting especially when lower socioeconomic status and age under 45 years. The intervention intensity is more important for

effectiveness than the delivery mode. Moderate changes in several lifestyle habits lead to good intervention results.⁸ In another novel randomized-controlled trial has indicated the Norfolk Diabetes Prevention lifestyle intervention reduced the risk of type 2 diabetes in current high-risk glycemic categories.²³ Smoking cessation treatment is one of the important lifestyle change strategies. Easy to use diabetes risk-prediction tools have a vital role in identifying those individuals who would benefit most from treatment.

Limitations and Suggestions for Future Studies

There were several limitations to this study. First, more than half of the smokers in the study could not be reached at the 6-month follow-up or refused to reply to questions by phone. Second, the initial BMI was assessed by the physician with a digital scale in the policlinic room but follow-up measurements were obtained from patients by phone. Thus, the relationship between weight gain and post-cessation diabetes risk development could not be evaluated perfectly. In future studies, addressing the postcessation period (activity, nutrition, anxiety cause of cessation treatment, nicotine withdrawal) may be more important, especially for new quitters.

Main points of the study

- Even if the FTND score is correlated with the diabetes risk score, both light and heavy smoking have similar diabetes risk before cessation treatment. However, the post-cessation period gets an increased T2DM risk among new quitters especially in favor of a high pre-treatment dependence level.
- The diabetes risk of the sixth-month followup among current smokers is 46% of new quitters (p=0.01 OR=0.46;0.25-0.86) A significant change in diabetes risk score is possible in the six-month cessation period between current smokers and quitters.
- Smoking cessation should be coupled with strategies for diabetes prevention and early detection for smokers at diabetes risk.

Informed consent

Verbal informed consent was obtained from all patients who participated in this study.

Conflict of Interest

No conflict of interest was declared by the authors.

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