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The Association Between Smoking Tobacco After a Diagnosis of Diabetes and the Prevalence of Diabetic Nephropathy in the Korean Male Population

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Objectives: Smoking is known to be associated with nephropathy in patients with diabetes. The distinct effects of smoking before and after diabetes has been diagnosed, however, are not well characterized. We evaluated the association of cigarette smoking before and after a diagnosis of diabetes with the presence of diabetic nephropathy.

Methods: We analyzed data from the 2011-2013 editions of the Korea National Health and Nutrition Examination Survey. A total of 629 male patients diagnosed with diabetes were classified as non-smokers (90 patients), former smokers (225 patients), or continuing smokers (314 patients). A "former smoker" was a patient who smoked only before receiving his diagnosis of diabetes. A "continuing smoker" was a patient who smoked at any time after his diabetes had been diagnosed. Diabetic nephropathy was defined as the presence of albuminuria (spot urine albumin/creatinine ratio ≥30 mg/g) or low estimated glomerular filtration rate (<60 mL/min/1.73 m^2). Multiple logistic regression models were used to assess the independent association after adjusting for age, duration of diabetes, hemoglobin A1c, body mass index, systolic blood pressure, medication for hypertension, and medication for dyslipidemia. Female patients were excluded from the study due to the small proportion of females in the survey who smoked.

Results: Compared to non-smokers, continuing smokers had significantly higher odds ratio ([OR], 2.17; 95% confidence interval [CI], 1.23 to 3.83) of suffering from diabetic nephropathy. The corresponding OR (95% CI) for former smokers was 1.26 (0.70 to 2.29).

Conclusions: Smoking after diagnosis of diabetes is significantly associated with the presence of diabetic nephropathy in the Korean male population.

Key words: Diabetes mellitus, Diabetic nephropathies, Smoking, Diagnosis

INTRODUCTION

Diabetic nephropathy is the leading cause of end-stage renal disease and is also responsible for cardiovascular mortality [1-3]. About 30% of patients with diabetes eventually develop diabetic nephropathy [1,4]. In Korea, diabetic nephropathy is becoming a substantial health care problem as the number of patients with diabetes is continuously increasing [5,6].

Albuminuria and a decline in the glomerular filtration rate (GFR) are commonly used for early detection of diabetic ne-

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phropathy. Increased urinary albumin is the earliest clinical feature of diabetic nephropathy. Gradual declines in GFR follow functional and structural changes of glomeruli [4,7].

Smoking has been reported to be associated with the progression of diabetic nephropathy. In prospective studies, progression to diabetic nephropathy was more frequent in smokers than non-smokers [8-10]. These studies classified subjects as non-smokers, former smokers and current smokers and found the hazard highest for current smokers. These findings suggest that continued smoking is related to the development of diabetic nephropathy.

Many studies have also evaluated the association between smoking cessation and diabetic nephropathy. A recent decline in diabetes-related complications, including end-stage renal disease, was linked to management and improvement of risk factors including smoking cessation [11]. Other prospective studies have reported that smoking cessation slowed the progression of diabetic nephropathy [12,13].

Smoking has a known association with nephropathy in the non-diabetic population. Subjects classified as smokers at the time of study had a significantly higher prevalence of albuminuria and abnormal renal function [14,15]. Therefore, smoking, whether before or after being diagnosed with diabetes, might be expected to increase an individual's risk of developing diabetic nephropathy. Previous studies, however, did not distinguish between the effect of smoking before and the effect of smoking after diagnosis. This study aims to make that distinction by considering the association between the presence of diabetic nephropathy and various smoking behaviors, specifically never smoking, smoking only before diagnosis, and smoking at any point in time after receiving a diagnosis of diabetes.

METHODS

We used data from the Korea National Health and Nutrition Examination Survey (KNHANES), a cross-sectional nationwide survey designed to assess the health and nutritional status of the Korean population [16]. The KNHANES selects a representative sample from the population and conducts personal interviews, physical examinations, and clinical and laboratory tests. Because the measurement of urinary albumin was introduced to the KNHANES in 2011, we used data from the 2011-2013 surveys. Females were excluded from our study because the reported prevalence of smoking among females in the survey was low. Moreover, research indicates that self-reports of smoking made by Asian females in similar surveys were unreliable [17]. Among the 9862 male participants during the three years, 708 subjects were reported to be diagnosed with diabetes by a physician. We excluded 79 subjects whose smoking status or other key variables were missing, leaving 629 male patients with diabetes in our data set. The KNHANES data were publicly available for research, so separate ethical approval by our institutional review board was not required.

Participants were classified as non-smokers, former smokers and current smokers based upon a smoking history taken as part of the survey. Within the class "former smokers", we estimated the date of smoking cessation using details included in the smoking history. Questions pertaining to smoking cessation changed during our study period, so we applied different methods when estimating smoking cessation dates from different subsets of the survey data. With survey data from 2011 to 2012, we added smoking duration to the age of smoking initiation. With data from 2013, we subtracted the duration of smoking cessation from current age. By comparing the age of smoking cessation and the age of diabetes diagnosis, we divided former smokers, as defined in the survey, into two groups. "Former smokers", as we define them, were those who smoked before the diagnosis of diabetes, but never after. "Continuing smokers" were those who smoked at any time after diagnosis of diabetes. By this definition, we included those reported to be current smokers in the KNHANES in our class "continuing smokers". Finally, KNHANES participants classified "non-smoker" were included in the class "non-smokers" in our study.

We adopted the definition and classification of chronic kidney diseases recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative to define diabetic nephropathy [18]. Diabetic nephropathy was defined as the presence of albuminuria or test results that show a low GFR. Presence of albuminuria was defined as a spot urine albumin/creatinine ratio (ACR) $\geq$30 mg/g, including microalbuminuria (30 - 299 mg/g) and macroalbuminuria ($\geq$300 mg/g). The Modification of Diet in Renal Disease formula was used to estimate the GFR: estimated GFR (mL/min/1.73 m^2) = $186.3 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ (if female). Low GFR was defined to be estimated GFR $<$60 mL/min/1.73 m^2.

We assessed known risk factors for diabetic nephropathy. They include age, duration of diabetes, hypertension, dyslipidemia, body mass index, systolic blood pressure, hemoglobin A1c (HbA1c), serum total cholesterol, and triglycerides. Duration of diabetes was calculated by taking the difference be-

tween the year of diabetes diagnosis and current age. Medication for hypertension or for dyslipidemia was self-reported. Body mass index was calculated by dividing weight in kilograms by squared height in meters. Because most of the participants reported that they used anti-diabetic medications to treat their diabetes, we used HbA1c <7.0% as our indicator of adequate glycemic control. Dyslipidemia was defined as serum total cholesterol ≥240 mg/dL, or serum triglyceride ≥ 200 mg/dL, or taking medication for dyslipidemia.

To begin our analysis, we classified subjects by our criteria for diabetic nephropathy. The 416 subjects that did not meet our criteria were labeled "normal". The 213 subjects that met our criteria were assigned the label "diabetic nephropathy". We then compared characteristics of the two groups and the prevalence of risk factors in the two groups. We performed Student's *t*-tests when response values were continuous and chi-square tests when values were categorical. Multiple logistic regression analysis was used to investigate the independent association between smoking before and after diagnosis of diabetes and the presence of diabetic nephropathy after adjusting for age, duration of diabetes, body mass index, HbA1c, systolic blood pressure, medication for hypertension, and the presence of dyslipidemia. We separately analyzed the association with each of our criteria for diabetic nephropathy: albuminuria and low GFR. In the analysis of albuminuria, a multinomial regression model was used. Albuminuria was subdivided into normoalbuminuria (ACR <30 mg/g), microalbuminuria (ACR=30-299 mg/g), and macroalbuminuria (ACR ≥300 mg/g). GFR <60 mL/min/1.73 m^2 was considered low. We repeated the analysis, regressing diabetic nephropathy against smoking history according to the life time smoking history (non-smokers, former smokers, and current smokers) and further dividing life time former smokers by their smoking duration (<20 years and ≥20 years). The *p*-value <0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The group of patients in our study, 629 male diagnosed with diabetes, is described by the basic characteristics recorded in Table 1. A large majority (85.7%) of patients smoked at some point in their lives. Among smokers, more than half (58.2%) continued smoking at some point after receiving their diagnosis of diabetes. Nearly 28% of all participants had albuminuria and slightly more than 12% had low GFR.

Table 1. Characteristics of 629 male patients with diabetes

Variables	Male patients with diabetes
Age (y)	62.5±10.4
Diabetes duration (y)	9.1±8.5
Hemoglobin A1c (%)	7.44±1.42
Body mass index (kg/m^2)	24.3±3.0
Systolic blood pressure (mmHg)	126.1±17.9
Smoking behavior	
Never smoked	90 (14.3)
Smoked only before diagnosis of diabetes	225 (35.8)
Ever smoked after diagnosis of diabetes	314 (49.9)
Medication for hypertension	
No	321 (51.0)
Yes	308 (49.0)
Dyslipidemia	
No	362 (57.5)
Yes	267 (42.5)
Urine albumin/creatinine ratio (mg/g)	
<30	455 (72.3)
≥30	174 (27.7)
Glomerular filtration rate (mL/min/1.73 m^2)[1]	
≥60	551 (87.6)
<60	78 (12.4)

Values are presented as mean±standard deviation or number (%).
[1]Glomerular filtration rate is estimated according to the Modification of Diet in Renal Disease formula.

The overall prevalence of diabetic nephropathy was 33.9% (n=213) (Table 2). Compared to patients without diabetic nephropathy, patients with diabetic nephropathy were significantly older, had suffered diabetes for a longer period of time, had higher systolic blood pressure, were more likely to exhibit inadequate glycemic control, and were more likely to take medication for hypertension. Smoking behavior after diagnosis of diabetes was significantly different, with a higher proportion of continuing smokers who smoked at any time after diagnosis of diabetes (56.8% vs. 46.4%; $p=0.009$) in the group of patients with diabetic nephropathy. There were no significant differences in body mass index and the presence of dyslipidemia between the two groups.

We then made these comparisons in a different way, comparing these characteristics and risks across groups defined by each of the two criteria for diabetic nephropathy, albuminuria and low GFR. When grouped by albuminuria, there were significant differences in age, duration of diabetes, systolic blood pressure, HbA1c, medication for hypertension and smoking

Table 2. Characteristics of 629 male patients with diabetes by presence of diabetic nephropathy, albuminuria and low GFR

Variables	Diabetic nephropathy (albuminuria[1] or low GFR[2])			Albuminuria			Low GFR		
	Normal (n=416)	Diabetic nephropathy (n=213)	*p*-value	Normal (n = 455)	Albuminuria (n = 174)	*p*-value	Normal (n = 551)	Low GFR (n = 78)	*p*-value
Age (y)	61.0±10.5	65.6±9.5	<0.001	61.6±10.6	64.9 ± 9.6	<0.001	61.8±10.3	67.8±9.5	<0.001
Duration of diabetes (y)	8.3±8.1	10.7±9.1	0.001	8.4±8.3	11.0 ± 8.9	0.001	8.8±8.2	11.6±10.4	0.02
BMI (kg/m^2)	24.3±2.9	24.3±3.1	0.99	24.3±2.9	24.3 ± 3.2	0.94	24.3±3.0	24.2±2.8	0.85
SBP (10 mmHg)	123.7±15.9	130.8±20.5	<0.001	123.6±15.6	132.6 ± 21.4	<0.001	126.0±17.8	126.6±18.7	0.81
HbA1c (%)									
<7.0	197 (47.4)	78 (36.6)	0.01	218 (47.9)	57 (32.8)	0.001	238 (43.2)	37 (47.4)	0.56
≥7.0	219 (52.6)	135 (63.4)		237 (52.1)	117 (67.2)		313 (56.8)	41 (52.6)	
Medication for hypertension									
No	237 (57.0)	84 (39.4)	<0.001	253 (55.6)	68 (39.1)	< 0.001	295 (53.5)	26 (33.3)	0.001
Yes	179 (43.0)	129 (60.6)		202 (44.4)	106 (60.9)		256 (46.5)	52 (66.7)	
Dyslipidemia[3]									
No	245 (58.9)	117 (54.9)	0.39	271 (59.6)	91 (52.3)	0.12	314 (57.0)	48 (61.5)	0.52
Yes	171 (41.1)	96 (45.1)		184 (40.4)	83 (47.7)		237 (43.0)	30 (38.5)	
Smoking behavior after diagnosis of diabetes									
Never smoked	67 (16.1)	23 (10.8)	0.009	71 (15.6)	19 (10.9)	0.002	80 (14.5)	10 (12.8)	0.76
Smoked only before diagnosis of diabetes	156 (37.5)	69 (32.4)		176 (38.7)	49 (28.2)		193 (35.0)	32 (41.0)	
Ever smoked after diagnosis of diabetes	193 (46.4)	121 (56.8)		208 (45.7)	106 (60.9)		278 (50.5)	36 (46.2)	

Values are presented as mean±standard deviation or number (%).
GFR, glomerular filtration rate; BMI, body mass index; SBP, systolic blood pressure; HbA1c, hemoglobin A1c.
[1]Albuminuria is defined as spot urine albumin/creatinine ratio ≥30 mg/g.
[2]Low GFR is defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2 according to the Modification of Diet in Renal Disease formula.
[3]Dyslipidemia includes those with total cholesterol ≥200 mg/dL, or triglyceride ≥150 mg/dL, or medication for dyslipidemia.

behavior after diagnosis of diabetes. When grouped by low GFR, there were significant differences in age, duration of diabetes, and medication for hypertension between the two groups.

Table 3 shows the association between smoking behavior after diagnosis of diabetes and the presence of diabetic nephropathy. The unadjusted odds ratio (OR) and 95% confidence intervals (CI) show that older age, longer duration of diabetes, higher systolic blood pressure, higher HbA1c, and taking medication for hypertension were significantly associated with the presence of diabetic nephropathy. After adjusting for all other variables, duration of diabetes and medication for hypertension became insignificant. The unadjusted OR (95% CI) for former smokers who had smoked only before their diagnosis of diabetes was 1.29 (0.74 to 2.24), and the adjusted OR was 1.23 (0.68 to 2.21). The unadjusted OR (95% CI) of continuing smokers who smoked at any time after diagnosis was 1.83 (1.08 to 3.09). The OR remained significant after adjusting for all covariates (adjusted OR, 2.12; 95% CI, 1.20 to 3.73).

Table 4 shows the association of smoking behavior after a diagnosis of diabetes with selected levels of albuminuria and with low GFR. The adjusted OR (95% CI) of smoking at any time after diabetes diagnosis, relative to normoalbuminuria, were 1.93 (1.01 to 3.69) for microalbuminuria and 3.60 (1.09 to 11.85) for macroalbuminuria. The corresponding OR (95% CI) for low GFR was 1.18 (0.54 to 2.55).

In the analysis classifying life time former smokers by their smoking duration, the adjusted OR (95% CI) for former smokers who smoked <20 years, former smokers who smoked ≥ 20 years, and current smokers were 1.15 (0.58 to 2.28), 1.54 (0.85 to 2.80) and 2.42 (1.33 to 4.39), respectively (Supplemental Table 1).

Table 3. Association between smoking behavior after diagnosis of diabetes and presence of diabetic nephropathy among patients with diabetes

Variables	Total	Diabetic nephropathy[1]	Unadjusted	Adjusted[2]
Age (10 y)	629	213 (33.9)	1.60 (1.34, 1.91)	1.62 (1.31, 2.02)
Duration of diabetes (10 y)			1.38 (1.14, 1.67)	1.13 (0.91, 1.41)
Hemoglobin A1c (%)			1.16 (1.04, 1.30)	1.21 (1.07, 1.38)
Body mass index (kg/m^2)			1.00 (0.95, 1.06)	1.03 (0.97, 1.10)
Systolic blood pressure (10 mmHg)			1.25 (1.14, 1.38)	1.22 (1.10, 1.35)
Medication for hypertension				
No	321	84 (26.2)	1.00 (reference)	1.00 (reference)
Yes	308	129 (41.9)	2.03 (1.45, 2.85)	1.40 (0.95, 2.06)
Dyslipidemia[3]				
No	362	117 (32.3)	1.00 (reference)	1.00 (reference)
Yes	267	96 (36.0)	1.18 (0.84, 1.64)	1.05 (0.72, 1.53)
Smoking behavior				
Never smoked	90	23 (25.6)	1.00 (reference)	1.00 (reference)
Smoked only before diagnosis of diabetes	225	69 (30.7)	1.29 (0.74, 2.24)	1.23 (0.68, 2.21)
Ever smoked after diagnosis of diabetes	314	121 (38.5)	1.83 (1.08, 3.09)	2.12 (1.20, 3.73)

Values are presented as number (%) or odds ratio (95% confidence interval).
[1]Diabetic nephropathy is defined as spot urine albumin/creatinine ratio ≥30 mg/g or estimated glomerular filtration rate <60 mL/min/1.73 m^2.
[2]Adjusted for other variables in the table (age, duration of diabetes, hemoglobin A1c, body mass index, systolic blood pressure, medication for hypertension, dyslipidemia, and smoking behavior).
[3]Dyslipidemia includes total cholesterol ≥200 mg/dL, or triglyceride ≥150 mg/dL, or taking medication for dyslipidemia.

Table 4. The association between smoking and presence of albuminuria and low glomerular filtration rate

Variables	Total	Urine albumin/creatinine ratio[1]				Glomerular filtration rate[2]	
		30 - 299 mg/g		≥300 mg/g		<60 mL/min/1.73 m^2	
Smoking behavior							
Never smoked	90	15 (16.7)	1.00 (reference)	4 (4.4)	1.00 (reference)	10 (11.1)	1.00 (reference)
Smoked only before diagnosis of diabetes	225	40 (17.8)	0.99 (0.50, 1.98)	9 (4.0)	1.28 (0.34, 4.75)	32 (14.2)	1.34 (0.61, 2.96)
Ever smoked after diagnosis of diabetes	314	73 (23.3)	1.93 (1.01, 3.69)	33 (10.5)	3.60 (1.09, 11.85)	36 (11.5)	1.18 (0.54, 2.55)

Values are presented as number (%) or odds ratio (95% confidence interval).
Each model was adjusted for age, duration of diabetes, hemoglobin A1c, body mass index, systolic blood pressure, medication for hypertension, and dyslipidemia. Dyslipidemia includes those with total cholesterol ≥200 mg/dL, or triglyceride ≥150 mg/dL, or medication for dyslipidemia.
[1]The reference group for multivariate logistic regression is urine albumin/creatinine ratio <30 mg/g.
[2]The reference group for multiple logistic regression is glomerular filtration rate ≥60 mL/min/1.73 m^2.

DISCUSSION

In this study we evaluated the association between smoking behavior and the presence of diabetic nephropathy, classifying smoking behavior relative to the date of diabetes diagnosis. Cigarette smoking, especially smoking that continued after a diagnosis of diabetes was independently associated with the presence of diabetic nephropathy.

In the literature, smoking was related with adverse outcomes on glomerular structure and function for patients with diabetes. Compared with nonsmoking patients with diabetes, smoking patients with diabetes had higher albumin excretion rates and thicker glomerular basement membranes [19]. The incidence or progression rate of diabetic nephropathy was higher in smokers than non-smokers [9,10]. In these studies the risk of nephropathy was highest for current smokers, followed by former smokers and non-smokers. This finding suggests that smoking, particularly continuous smoking, is associated with diabetic nephropathy.

Smoking also increases the risk of albuminuria or renal dysfunction in the non-diabetic population. According to some cross-sectional studies of non-diabetic persons, smoking was

related with the presence of albuminuria or low GFR [14,20]. Smoking was also associated with increased prevalence of proteinuria in repeated health screening examinations [21]. In some of these studies, daily amounts of smoking showed a dose-response relationship with albuminuria [14,21]. Smoking exposure seems to be related with diabetic nephropathy, regardless of the point in time that the exposure occurred, before or after the onset of diabetes. In our results, the OR for former smokers who smoked only before diagnosis of diabetes was higher than for non-smokers but lower than for smokers who smoked at any time after receiving their diagnosis of diabetes. Therefore we conclude that smoking exposure, especially when diabetes is prevalent, is associated with diabetic nephropathy.

Some studies have suggested that smoking cessation can delay the progression of diabetic nephropathy. Lower progression to diabetic nephropathy or improvement of the ACR in former smokers had been observed in prospective studies of diabetic subjects who exhibited microalbuminuria [12,13,22]. It has been reported that total smoking pack-years showed a dose response relationship with the prevalence of diabetic nephropathy among former smokers [9,23]. A prospective study that focused on the relationship of smoking pack-years and the incidence of diabetes showed a similar result. In this study, the hazard of diabetes was higher as smoking pack-years increased and when the time since smoking cessation was shorter [24]. This dose-response relationship was partially shown in our analysis. When we stratified former smokers by smoking duration, the OR was higher for the group formed of those who smoked for longer periods of time. We could not expand the analysis to include subjects identified as current smokers in KNHANES, due to incomplete smoking duration information in the survey. We also considered the association of time between smoking cessation and diabetes diagnosis with the presence of diabetic nephropathy among former smokers (data not shown). The regression indicated a higher OR when the time interval was shorter, but the result was not statistically significant. To more fully reveal the effect of smoking, further prospective studies evaluating smoking in conjunction with diabetes and with diabetic complications will be required.

The pathogenesis of diabetic nephropathy from diabetes stems from high blood glucose and blood lipid levels. High blood glucose and lipids increase oxidative stress and induce inflammation of renal structures [25,26]. Smoking is associated with high blood lipids, and independently increases oxidative stress [27-29]. We assume that smoking participates in the development of diabetic nephropathy by mediating its progression along these pathways. Moreover, smokers take actions that exacerbate the impact of smoking. They have been shown to be unaware of the progression of a chronic disease, leading to low levels of treatment for that disease. Even when they are aware of disease, they, frequently, continue smoking. [30,31]. If the same pattern of behavior holds with diabetes, the delay in diagnosis and the delay in treatment increases the likelihood of complications. Microvascular complications may have already progressed by the time they receive a diagnosis of diabetes. If nothing else, delayed diagnosis and treatment results in prolonging the time in which the patient suffers in a hyperglycemic state [32]. Based on the literature and our findings, we conclude that smoking is independently associated with diabetic nephropathy, and that the impact is higher when diabetes is prevalent. We also cautiously interpret the literature and our findings to indicate that smoking cessation in patients with diabetes may delay the progression of diabetic nephropathy or slow the decrease of glomerular function.

When we grouped subjects separately by albuminuria and then by low GFR, rather than by diabetic nephropathy, we found that the prevalence of albuminuria was significantly higher among those that smoked at any point in time after diagnosis of diabetes. This finding was consistent with many other studies which evaluated smoking and albuminuria [8,20]. The distribution of smoking behavior, however, was not significantly different for those with normal and low GFR in our results. We do not know the exact reason for this, but some studies have reported that smoking can be related to either decreased or increased GFR [14,33]. They explained that smoking acutely induces a decrease in renal plasma flow, but that these repeated episodes alter the structure of glomerular vessels and result in hyperfiltration [14,34]. We assume that these conflicting effects of smoking over time have been mixed in our cross-sectional analysis.

There are several limitations to our study. First, we could not establish causal relationships between smoking behavior and diabetic nephropathy due to the cross-sectional study design. We could not determine whether smoking was associated with the early development or progression of diabetic nephropathy. Second, participation in the KNHANES was limited to non-institutionalized, community-dwelling individuals [35]. This may have led to the exclusion of patients with diabetes and advanced stages of diabetic nephropathy. Moreover, our

study excluded female participants, and so, its results cannot be generalized to the entire diabetic population. Third, our study was limited to those diagnosed with diabetes by a physician. We required the diagnosis date. The 2011-2013 KNHANES surveys included 755 subjects who were undiagnosed but satisfied the diagnostic criteria for diabetes (fasting blood glucose ≥126 mg/dL or HbA1c ≥6.5%) based on blood tests [36]. While these individuals were not included in our study, we confirmed that they exhibited smoking behavior similar to that of our subjects. Therefore, we assume that the results of a study that included these undiagnosed individuals would be consistent with the results of this current study. Fourth, we used the date of diagnosis rather than diabetes onset in our study. In some cases diabetes could have been present for many years before diagnosis and diabetic nephropathy could have been present when diabetes was diagnosed [4]. However, the date of diagnosis still has a clinical implication. It may have been used to persuade diabetic smokers to quit. Fifth, the effect of covariates might not be well controlled. There were confounding factors which we could not include. KNHANES 2013 lacked information needed to estimate smoking duration for current smokers, and the 2011 and 2012 surveys did not ask participants about their daily tobacco consumption. In addition, we had incomplete data regarding insulin resistance. Serum insulin was not measured in KNHANES after 2011 [22]. Finally, our study did not clearly distinguish between type 1 diabetes and type 2 diabetes. We do know, however, that the proportion of diabetics with type 1 diabetes is small in Korea [37].

In conclusion, smoking after a diagnosis of diabetes is associated with the presence of diabetic nephropathy. Prospective research studies, evaluating the effect of smoking on diabetic nephropathy are required.

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CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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Supplemental Table 1. The association between smoking behavior and duration, and presence of diabetic nephropathy

Variables	Total	Diabetic nephropathy[1]	Unadjusted	Adjusted[2]
Smoking behavior				
Non-smoker	90	23 (25.6)	1.00 (reference)	1.00 (reference)
Former smoker: smoking duration (y)				
<20	102	30 (29.4)	1.21 (0.64, 2.29)	1.15 (0.58, 2.28)
≥20	205	74 (36.1)	1.65 (0.95, 2.86)	1.54 (0.85, 2.80)
Current smoker	225	85 (37.8)	1.77 (1.03, 3.05)	2.42 (1.33, 4.39)

Values are presented as number (%) or odds ratio (95% confidence interval). Total 7 subjects were further excluded in this analysis due to the lack of smoking duration.
[1]Diabetic nephropathy is defined as spot urine albumin/creatinine ratio ≥30 mg/g or estimated glomerular filtration rate <60 mL/min/1.73 m^2 according to the Modification of Diet in Renal Disease formula.
[2]Adjusted for age, duration of diabetes, hemoglobin A1c, body mass index, systolic blood pressure, medication for hypertension, and dyslipidemia. Dyslipidemia includes those with total cholesterol ≥200 mg/dL, or triglyceride ≥150 mg/dL, or medication for dyslipidemia.