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Clinical Research Article

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Association Between Smoking Behavior and Insulin Resistance Using Triglyceride-Glucose Index Among South Korean Adults

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Abbreviations: BMI, body mass index; e-cigarette, electronic cigarette; HOMA-IR, homeostasis model assessment of insulin resistance; KNHANES VII, 2016-2018 Korea National Health and Nutrition Examination Survey; OR, odds ratio; T2DM, type 2 diabetes mellitus; TyG index, triglyceride-glucose index.

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Abstract

Context: Insulin resistance is a determinant of diabetes. With the increasing popularity of electronic smoking, the number of dual smokers (smoking both cigarettes and electronic cigarettes [e-cigarettes]) is increasing. However, few studies have assessed the association between insulin resistance and smoking behavior, including dual smoking.

Objective: This work aims to investigate the association between smoking behaviors and insulin resistance.

Methods: This prospective, cross-sectional study took place among the general community. A total of 11 653 participants (4721 male and 6932 female) aged 19 years or older from the 2016 to 2018 Korea National Health and Nutrition Examination Survey were divided based on their smoking behaviors: dual smokers (both cigarettes and e-cigarettes), single smokers (cigarette smokers), previous smokers, and nonsmokers. Insulin resistance was determined based on the triglyceride-glucose index. Multiple logistic regression analysis was performed to investigate the association between smoking behavior and insulin resistance.

Results: Among the participants, 164 males (3.5%) and 33 females (0.5%) were dual-smokers, and 1,428 males (30.2%) and 308 females (4.4%) were single-smokers. Male and female smokers (dual and single) both had higher odds of being in a group with higher insulin resistance than nonsmokers (male, dual: OR = 2.19; 95% CI, 1.39-3.44; single: OR = 1.78; 95% CI, 1.43-2.22; female, dual: OR = 2.32; 95% CI, 1.01-5.34; single: OR = 1.76; 95% CI, 1.28-2.42).

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Conclusion: This study suggests that single and dual smoking both may increase the risk of insulin resistance in the general population. Education on the adverse effects of smoking behaviors may be an important strategy to improve the health of the population.

Key Words: dual smoking, insulin resistance, KNHANES, tobacco, triglyceride-glucose index

Diabetes is one of the biggest public health problems in the world. Type 2 diabetes mellitus (T2DM) is the most common type of diabetes, accounting for about 90% of all diabetes cases (1). It is an important cause of cardiovascular disease, blindness, and kidney and neurological diseases and is directly associated with death worldwide; it is generally characterized by insulin resistance, a condition in which the body does not fully respond to insulin (1).

Insulin resistance is defined as an attenuated biological response produced by normal or elevated insulin levels (2); classically this refers to impaired sensitivity to insulin-mediated glucose disposal (3). Insulin resistance is a fundamental aspect of T2DM and is also related to various pathological and physiological aftereffects, including hyperlipidemia, hypertension, and cardiovascular disease (4).

Although there are standard methods for assessing insulin resistance such as a hyperinsulinemic euglycemic clamp, insulin suppression test, and insulin tolerance test, these tests are invasive and difficult to apply in the clinic because of their complexity and high cost (5). Therefore, insulin resistance is estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) (6), which is a simple, indirect indicator; however, recently, the triglyceride-glucose (TyG) index, based on triglyceride and fasting blood glucose levels, has been recommended as a useful indicator for insulin resistance (7, 8). Because insulin tests are not readily available and are expensive in most developing countries, the TyG index, which can be determined using a simple blood test, is a useful indicator of blood sugar and triglyceride levels in diabetes patients (7). Furthermore, previous studies have identified the TyG index as a useful tool for assessing insulin resistance (9, 10).

One of the lifestyle factors that can directly or indirectly affect insulin resistance is smoking (11). The smoking rate of Korean males is the fourth highest among those in Organisation for Economic Co-operation and Development countries (12). However, as part of the Korean government's efforts to reduce tobacco use, which included the recent increase in cigarette prices, the smoking rate has fallen from 66.3% in 1998 to 39.4% in 2015, and has continued to decline thus far (13). Electronic cigarettes (e-cigarettes) were introduced in Korea in 2007 as a healthy alternative to cigarettes or as a smoking cessation aid (13, 14). E-cigarettes are known to be associated with lower exposure to toxic substances than conventional cigarettes because they do not contain combustion products (15). Currently, the ever use of e-cigarettes is 6.6% in South Korea and 8.5% in the United States (16). However, most e-cigarette users do not stop smoking but rather use both e-cigarettes and cigarettes (dual smokers) (17).

Research on long-term toxicity of e-cigarettes is limited, and studies showing the efficacy of e-cigarettes as a healthier alternative to conventional cigarettes have shown mixed results (15). In particular, unlike previous studies reporting consistent results on the association between conventional smoking and insulin resistance (18, 19), the existing literature on the impact of e-cigarette use on insulin resistance is limited and shows inconsistent results. One study using experimental animal and human data showed that e-cigarettes use is not related to insulin resistance (20), whereas another study involving mice exposed to e-cigarettes showed that e-cigarettes have an effect similar to that of conventional cigarettes on insulin resistance (21).

The effectiveness of e-cigarettes as a healthier alternative to conventional cigarettes is not fully known, and it remains unclear whether these devices are safe for individuals interested in quitting or reducing smoking. Furthermore, the health effects of dual smoking, the use of both electronic and conventional cigarettes, are yet unknown, but it is likely that dual smoking causes tobacco dependence (22). There is not enough evidence to clarify the relationship between dual smoking or e-cigarette smoking and insulin resistance. Therefore, this study investigated the association of cigarette and dual smoking with the TyG index, a useful indicator for insulin resistance.

Materials and Methods

Data and Study Population

This study was based on data collected by the 2016 to 2018 Korea National Health and Nutrition Examination Survey (KNHANES VII) and the secondary analysis of a large data set. The KNHANES is a nationwide population-based cross-sectional survey that has been conducted annually in Korea since 1998; it is conducted under the direction of the Centers for Disease Control and Prevention of the Ministry of Health and Welfare to accurately assess national health and nutritional status, under Article 16 of the National Health Promotion Act (23).

The total number of respondents for the 2016 to 2018 period was 24 269. Information from individuals aged 1 to 18 years was excluded because KNHANES did not ask people younger than 19 years about cigarettes (N = 4880). In addition, participants who had been previously diagnosed with diabetes by a physician or who had been taking antidiabetic drugs and those with a glycated hemoglobin A_{1c} level of 6.5% or greater (48 mmol/mol) or a blood glucose level of 126.0 mg/dL or greater were excluded from the study sample to avoid confounding the insulin resistance–related analyses (N = 2575) (24-27). Furthermore, participants with missing data on variables were excluded (N = 5161). Finally, the data of 11 606 participants (male: 4721, and female: 6932) were analyzed. Use of the KNHANES data did not require prior consent from the respondents because the respondents' information was kept completely anonymous. Therefore, these data are publicly available, and their use does not require ethical approval.

Variables

Dependent variable

The main dependent variable in this study was the TyG index, a product of the fasting levels of triglycerides and glucose, which is a useful indicator of insulin resistance (8). In the KNHANES data, fasting blood samples (fasting after 1900 h the day before the investigation) were used for testing. The TyG index is calculated using the formula $\ln[\text{triglyceride (mg/dL)} \times \text{fasting blood glucose (mg/dL)}/2]$ and is expressed on a logarithmic scale (7).

Independent variable

The main independent variable was the smoking behavior of the participants, based on cigarette and e-cigarette use. In the survey, participants were asked whether they were currently using or had ever used cigarettes or e-cigarettes. Accordingly, we classified the participants into 4 categories: nonsmokers, ex-smokers, single smokers (only cigarettes), and dual smokers (both cigarettes and e-cigarettes). This classification was in accordance with that used in previous studies investigating smoking behaviors using the same survey instrument (27, 28).

Control variables

Control variables that can act as potential confounding variables include socioeconomic and health-related factors. In this study, the evaluated socioeconomic characteristics included age, marital status, education level, household income level, region, and occupation. Health-related characteristics included waist circumference, body mass index (BMI), drinking status, walking frequency, chronic diseases, family history, medication use, pack-years, and total calorie intake.

Statistical Analysis

In this study, all statistics were calculated using sample weights assigned to study participants. The sample weights were constructed by the KNHANES to represent the Korean population by accounting for the complex survey design and survey nonresponse (29). Before the analysis, participants were classified into the following insulin resistance groups according to the median TyG index (8.5): low insulin resistance group (< 8.5) and high insulin resistance group (≥ 8.5) (24, 30). In addition, to estimate valid cutoff values, the TyG index was further analyzed using the receiver operating characteristic curve for impaired fasting glucose; an effective cutoff value of 8.5143 was found. Therefore, a TyG index of 8.5 was judged to be an appropriate threshold for differentiation between high and low insulin resistance. Univariate linear regression was used to assess the association of cigarette type with insulin resistance, socioeconomic and health-related variables, and survey year. Multiple regression analysis was performed while controlling for covariates to analyze the association between cigarette type and insulin resistance. Subgroup analyses were performed with multiple linear regression stratified by sex to investigate the associations of waist circumference, BMI, drinking status, walking frequently, and chronic diseases with insulin resistance. Odds ratios (ORs) and 95% CIs were calculated by comparing nonsmokers to ex-smokers, single smokers, and dual smokers.

All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc). Statistical results were considered significant at a *P* value of less than .05.

Results

Table 1 presents the general characteristics of the study population. Of the 11 653 participants, 4721 were male (40.5%) and 6932 were female (59.5%). Of the 4721 males, 164 (3.5%) were dual smokers, 1428 (30.2%) were single smokers, 1892 were ex-smokers (40.1%), and 1237 (26.2%) were nonsmokers. Of the 6932 females, 33 (0.5%) were dual smokers, 308 (4.4%) were single smokers, 420 were ex-smokers (6.1%), and 6171 (89.0%) were nonsmokers.

Table 2 shows the association between smoking behavior and insulin resistance in male and female participants after adjusting for all control variables. Male and female participants who were dual smokers or single smokers were at a higher risk of increased insulin

Table 1. General characteristics of the study population

Variables	Total		Male					Female				
			Low (< 8.5)		High(≥ 8.5)		P	Low (< 8.5)		High(≥ 8.5)		P
	No.	%	No.	%	No.	%		No.	%	No.	%	
Total	11 653	100.0	1744	15.0	2977	25.55		4232	36.3	2700	23.17	
Smoking behavior							< .0001					.0066
Dual smoker	197	1.7	40	2.3	124	4.2		19	0.4	14	0.5	
Single smoker	1736	14.9	427	24.5	1001	33.6		160	3.8	148	5.5	
Ex-smoker	2312	19.8	703	40.3	1189	39.9		267	6.3	153	5.7	
Nonsmoker	7408	63.6	574	32.9	663	22.3		3786	89.5	2385	88.3	
Age							< .0001					< .0001
19-29	1624	13.9	400	22.9	345	11.6		732	17.3	147	5.4	
30-39	2190	18.8	308	17.7	567	19.0		972	23.0	343	12.7	
40-49	2449	21.0	254	14.6	670	22.5		983	23.2	542	20.1	
50-59	2213	19.0	251	14.4	586	19.7		754	17.8	622	23.0	
60-69	1813	15.6	271	15.5	491	16.5		472	11.2	579	21.4	
≥ 70	1364	11.7	260	14.9	318	10.7		319	7.5	467	17.3	
Marital status							< .0001					.0178
Married	8188	70.3	1118	64.1	2210	74.2		2923	69.1	1937	71.7	
Single. widow, divorced, separated	3465	29.7	626	35.9	767	25.8		1309	30.9	763	28.3	
Educational level							< .0001					
Middle school or less	924	7.9	365	20.9	559	18.8			0.0		0.0	
High school	1627	14.0	650	37.3	977	32.8			0.0		0.0	
College or more	2170	18.6	729	41.8	1441	48.4			0.0		0.0	
Household income							.0050					< .0001
Low	1726	14.8	274	15.7	371	12.5		518	12.2	563	20.9	
Mid-low	2794	24.0	410	23.5	683	22.9		970	22.9	731	27.1	
Mid-high	3404	29.2	514	29.5	885	29.7		1276	30.2	729	27.0	
High	3729	32.0	546	31.3	1038	34.9		1468	34.7	677	25.1	
Region							.8891					< .0001
Urban area	9651	82.8	1426	81.8	2439	81.9		3606	85.2	2180	80.7	
Rural area	2002	17.2	318	18.2	538	18.1		626	14.8	520	19.3	
Occupational categories[b]							< .0001					< .0001
White	3284	28.2	500	28.7	1016	34.1		1281	30.3	487	18.0	
Pink	1533	13.2	166	9.5	318	10.7		641	15.1	408	15.1	
Blue	2541	21.8	593	34.0	945	31.7		561	13.3	442	16.4	
Inoccupation	4295	36.9	485	27.8	698	23.4		1749	41.3	1363	50.5	
Waist circumference[g]							< .0001					< .0001
Abdominal obesity	7968	68.4	653	37.4	1904	64.0		3664	86.6	1747	64.7	

Table 1. Continued

Variables	Triglycerides-glucose index											
	Total		Male					Female				
			Low (< 8.5)		High(≥ 8.5)		*P*	Low (< 8.5)		High(≥ 8.5)		*P*
	No.	%	No.	%	No.	%		No.	%	No.	%	
Normal	3649	31.3	1091	62.6	1037	34.8		568	13.4	953	35.3	
BMI[d]							< .0001					< .0001
Underweight or normal, < 23.0	5293	45.4	824	47.2	762	25.6		2739	64.7	968	35.9	
Overweight, 23.0-24.9	2641	22.7	453	26.0	792	26.6		734	17.3	662	24.5	
Obese, ≥ 25.0	3719	31.9	467	26.8	1423	47.8		759	17.9	1070	44.1	
Drinking status							< .0001					< .0001
No	2878	24.7	318	18.2	396	13.3		1145	27.1	1019	37.7	
Yes	8775	75.3	1426	81.8	2581	86.7		3087	72.9	1681	62.3	
Walking frequently[c]							< .0001					< .0001
Inadequate	6360	54.6	820	47.0	1600	53.7		2286	54.0	1654	61.3	
Adequate	5293	45.4	924	53.0	1377	46.3		1946	46.0	1046	38.7	
Chronic diseases[e]							< .0001					< .0001
No	8807	75.6	1389	79.6	2145	72.1		3540	83.6	1733	64.2	
Yes	2846	24.4	355	20.4	832	27.9		692	16.4	967	35.8	
Family history[h]							.0003					.7906
No	9525	81.7	1500	86.0	2439	81.9		3406	80.5	2180	80.7	
Yes	2128	18.3	244	14.0	538	18.1		826	19.5	520	19.3	
Medication[i]							.0009					< .0001
No	9397	80.6	1446	82.9	2350	78.9		3676	86.9	1925	71.3	
Yes	2256	19.4	298	17.1	627	21.1		556	13.1	775	28.7	
Year							.5651					.4358
2016	4216	36.2	557	31.9	935	31.4		1379	32.6	904	33.5	
2017	4348	37.3	573	32.9	1023	34.4		1420	33.6	866	32.1	
2018	4453	38.2	614	35.2	1019	34.2		1433	33.9	930	34.4	
Pack-year[a]	5.6	12.5	11.1	16.4	14.2	16.7	.0007	0.45	2.87	0.74	3.78	< .0001
Total kcal[a,f]	187 795.1	80 659.3	22 0842.0	88 629.3	218 301.9	84 382.2	.0009	168 568.9	70 151.6	162 948.2	67 224.3	.3335

[a]Data for pack-year and total calorie intake are presented as the mean and SD.
[a]Three groups (white, pink, blue) based on the International Standard Classification of Occupations codes. The inoccupation group includes homemakers.
[c]Walking frequency: based on the recommended walking activity according to the physical activity guidelines in Korea.
[d]BMI, body mass index; obesity status was defined based on BMI according to the 2018 Clinical Practice Guidelines for Overweight and Obesity in Korea.
[e]Chronic disease was defined as diagnosed diseases, such as hypertension and dyslipidemia.
[f]Total energy intake = (carbohydrate (g) × 4 kcal/g) + (protein (g) × 4 kcal/g) + (fat (g) × 9 kcal/g).
[g]Waist circumference was determined using the Korean abdominal obesity criteria: 90 cm for men and 85 cm for women.
[h]Family history of diabetes was defined as having an immediate family member (eg, father, mother, brother, and/or sister) with diabetes.
[i]Medication use was defined as taking medications to treat hypertension and dyslipidemia.

Table 2. Association between smoking behaviors and the triglyceride-glucose index

Variables	TyG index (> 8.5)			
	Male		Female	
	OR	95% CI	OR	95% CI
Smoking behavior				
Dual smoker	2.19	(1.39-3.44)	2.32	(1.01-5.34)
Single smoker	1.78	(1.43-2.22)	1.76	(1.28-2.42)
Ex-smoker	1.17	(0.95-1.43)	1.20	(0.89-1.60)
Nonsmoker	1.00		1.00	
Age				
19-29	1.00		1.00	
30-39	1.62	(1.21-2.17)	1.52	(1.16-2.00)
40-49	2.25	(1.64-3.10)	2.24	(1.71-2.94)
50-59	2.06	(1.48-2.85)	3.07	(2.32-4.07)
60-69	1.66	(1.16-2.36)	3.40	(2.48-4.66)
≥ 70	1.07	(0.68-1.67)	3.57	(2.51-5.07)
Marital status				
Married	1.00		1.00	
Single, widow, divorced, separated	0.91	(0.73-1.15)	1.07	(0.90-1.27)
Educational level				
Middle school or less	1.00		1.00	
High school	0.91	(0.71-1.16)	1.02	(0.83-1.25)
College or more	0.99	(0.75-1.30)	0.92	(0.73-1.16)
Household income				
Low	1.00		1.00	
Mid-low	1.12	(0.84-1.51)	0.96	(0.76-1.20)
Mid-high	1.09	(0.81-1.48)	0.95	(0.75-1.19)
High	1.17	(0.86-1.57)	0.83	(0.65-1.05)
Region				
Urban area	1.00		1.00	
Rural area	1.12	(0.88-1.42)	1.09	(0.91-1.29)
Occupational categories[a]				
White	0.83	(0.65-1.06)	0.90	(0.76-1.06)
Pink	0.80	(0.60-1.06)	0.85	(0.71-1.02)
Blue	0.58	(0.46-0.73)	0.70	(0.58-0.85)
Inoccupation	1.00		1.00	
Waist circumference[f]				
Abdominal obesity	2.09	(1.69-2.58)	1.57	(1.30-1.91)
Normal	1.00		1.00	
BMI[c]				
Underweight or normal, < 23.0	1.00		1.00	
Overweight, 23.0-24.9	1.36	(1.11-1.67)	2.01	(1.72-2.36)
Obese, ≥25.0	1.94	(1.51-2.49)	2.66	(2.20-3.20)
Drinking status				
No	1.00		1.00	
Yes	1.41	(1.12-1.78)	0.85	(0.74-0.98)
Walking frequently[b]				
Inadequate	1.00		1.00	
Adequate	0.75	(0.64-0.88)	0.89	(0.78-1.01)
Chronic diseases[d]				
No	1.00		1.00	
Yes	2.14	(1.50-3.04)	1.90	(1.42-2.55)
Family history[g]				
No	1.00		1.00	
Yes	1.09	(0.90-1.31)	1.14	(0.98-1.33)

Table 2. Continued

Variables	TyG index (> 8.5)			
	Male		Female	
	OR	95% CI	OR	95% CI
Medication[b]				
No	1.00		1.00	
Yes	0.54	(0.37-0.79)	0.64	(0.47-0.88)
Year				
2016	1.00		1.00	
2017	1.13	(0.94-1.37)	0.89	(0.76-1.05)
2018	0.97	(0.81-1.18)	1.01	(0.87-1.18)
Pack-year[a]	1.00	(1.00-1.01)	0.99	(0.97-1.02)
Total kcal[e]	**1.00**	(1.00-**1.00**)	**1.00**	(1.00-**1.00**)

Abbreviations: OR, odds ratio; TyG index, triglyceride-glucose index.
[a]Three groups (white, pink, blue) based on the International Standard Classification of Occupations codes. The inoccupation group includes homemakers.
[b]Walking frequency: based on the recommended walking activity according to the physical activity guidelines in Korea.
[c]BMI, body mass index; obesity status was defined based on BMI according to the 2018 Clinical Practice Guidelines for Overweight and Obesity in Korea.
[d]Chronic disease was defined as diagnosed diseases, such as hypertension and dyslipidemia.
[e]Total energy intake = (carbohydrate (g) × 4 kcal/g) + (protein (g) × 4 kcal/g) + (fat (g) × 9 kcal/g).
[f]Waist circumference was determined using the Korean abdominal obesity criteria: 90 cm for men and 85 cm for women.
[g]Family history of diabetes was defined as having an immediate family member (eg, father, mother, brother, and/or sister) with diabetes.
[h]Medication use was defined as taking medications to treat hypertension and dyslipidemia.

resistance than nonsmokers. Among the male participants, compared with nonsmokers, dual smokers (OR = 2.19; 95% CI, 1.39-3.44) and single smokers (OR = 1.78; 95% CI, 1.43-2.22) showed significant associations with insulin resistance. Among the female participants, compared with nonsmokers, dual smokers (OR = 2.32; 95% CI, 1.01-5.34) and single smokers (OR = 1.76; 95% CI, 1.28-2.42) showed significant associations with insulin resistance.

Table 3 shows the results of the subgroup analysis stratified by independent variables. Using the nonsmoker group as a reference, we found that male and female participants in the dual-smoker group and single-smoker group who consumed alcohol (male, dual: OR = 2.34 [95% CI, 1.44-3.18], single: OR = 1.73 [95% CI, 1.36-2.19]; female, dual: OR = 2.32 [95% CI, 1.09-5.68], single: OR = 1.78 [95% CI, 1.26-2.52]) and walked infrequently (male, dual: OR = 2.19 [95% CI, 1.17-4.08], single: OR = 2.01 [95% CI, 1.48-2.72]; female, dual: OR = 3.26 [95% CI, 1.09-9.78], single: OR = 1.64 [95% CI, 1.06-2.56]) had a high risk of insulin resistance. In those with chronic diseases, the risk of insulin resistance increased in the dual-smoker and single-smoker groups both for male and female participants, but the increase was significant only in male participants (male, dual: OR = 2.14 [95% CI, 1.30-3.52], single: OR = 1.70 [95% CI, 1.33-2.18]). With respect to BMI, male dual smokers and single smokers in the obesity group showed the highest risk of insulin resistance (dual: OR = 2.56 [95% CI, 1.28-5.12], single: OR = 2.25 [95% CI, 1.56-3.24]); female dual smokers and single smokers in the underweight/normal weight group had the highest risk of insulin resistance (dual: OR = 3.65 [95% CI, 1.28-10.28], single: OR = 1.62 [95% CI, 1.03-2.56]). With respect to waist circumference, the risk of insulin resistance was high in male dual smokers and single smokers in the abdominal obesity group, using the nonsmoker group as a reference (dual: OR = 2.34 [95% CI, 1.20-4.54], single: OR = 1.73 [95% CI, 1.29-2.33]).

Discussion

It is widely known that smoking negatively affects an individual's overall health (31). This study aimed to investigate the association between smoking behavior and insulin resistance based on the TyG index in Koreans using representative data from the KNHANES. We also performed a subgroup analysis using health-related factors related to insulin resistance: waist circumference, BMI, drinking status, walking frequency, and chronic disease. This is one of the few studies that have investigated the relationship between smoking behavior and insulin resistance using the TyG index, a useful surrogate marker for insulin resistance.

We observed that smoking behaviors such as dual smoking and single smoking were associated with insulin resistance risk. In addition, we found that dual smoking was significantly associated with the highest probability of insulin resistance. However, these results are contrary to those of previous studies that examined the relationship between insulin resistance and smoking behavior using the HOMA-IR (20, 32). According to the results of this study,

Table 3. Subgroup analyses stratified by independent variables

Variables	Triglycerides-glucose index						
	Smoking behavior						
	None	Dual smoker		Single smoker		Ex-smoker	
	OR	OR	95% CI	OR	95% CI	OR	95% CI
Male							
Waist circumference							
Abdominal obesity	**1.00**	2.34	(1.20-4.54)	1.73	(1.29-2.33)	1.02	(0.78-1.35)
Normal	**1.00**	2.04	(1.14-3.64)	1.84	(1.33-2.54)	1.30	(0.96-1.80)
BMI[a]							
Underweight or normal, < 23.0	**1.00**	1.88	(0.83-4.25)	1.41	(0.99-2.01)	0.93	(0.66-1.31)
Overweight, 23.0-24.9	**1.00**	1.58	(0.64-3.91)	1.69	(1.09-2.62)	1.10	(0.75-1.63)
Obese, ≥25.0	**1.00**	2.56	(1.28-5.12)	2.25	(1.56-3.24)	1.47	(1.03-2.08)
Drinking status							
No	**1.00**	0.61	(0.14-2.78)	2.21	(1.12-4.36)	1.44	(0.86-2.40)
Yes	**1.00**	2.34	(1.44-3.81)	1.73	(1.36-2.19)	1.12	(0.89-1.41)
Walking frequently[b]							
Inadequate	**1.00**	2.19	(1.17-4.08)	2.01	(1.48-2.72)	1.22	(0.92-1.62)
Adequate	**1.00**	2.14	(1.08-4.23)	1.53	(1.10-2.13)	1.10	(0.82-1.48)
Chronic diseases[c]							
No	**1.00**	2.00	(0.71-5.65)	2.32	(1.32-4.07)	1.09	(0.86-1.38)
Yes	**1.00**	2.14	(1.30-3.52)	1.70	(1.33-2.18)	1.70	(1.07-2.68)
Female							
Waist circumference							
Abdominal obesity	1.00	26.34	(2.67-262.02)	1.86	(0.85-4.04)	0.94	(0.55-1.62)
Normal	1.00	1.94	(0.70-5.35)	1.68	(1.18-2.39)	1.24	(0.89-1.73)
BMI[a]							
Underweight or normal, < 23.0	1.00	3.65	(1.28-10.28)	1.62	(1.03-2.56)	1.35	(0.88-2.08)
Overweight, 23.0-24.9	1.00	1.94	(0.16-23.58)	1.48	(0.72-3.04)	0.89	(0.51-1.55)
Obese, ≥ 25.0	1.00	1.31	(0.33-5.16)	2.31	(1.20-4.42)	1.26	(0.74-2.14)
Drinking status							
No	1.00	2.02	(0.33-12.25)	1.91	(0.72-5.11)	0.90	(0.47-1.71)
Yes	1.00	2.32	(1.09-5.68)	1.78	(1.26-2.52)	1.24	(0.89-1.72)
Walking frequently[b]							
Inadequate	1.00	3.26	(1.09-9.78)	1.64	(1.06-2.56)	1.28	(0.87-1.88)
Adequate	1.00	1.85	(0.45-7.52)	2.01	(1.22-3.31)	1.16	(0.72-1.85)
Chronic diseases[c]							
No	1.00	1.79	(0.69-4.63)	1.53	(1.05-2.22)	1.17	(0.84-1.62)
Yes	**1.00**	3.18	(0.39-26.18)	1.75	(0.73-4.22)	1.12	(0.54-2.33)

Abbreviation: OR, odds ratio.
[a]BMI, body mass index; obesity status was defined based on BMI according to the 2018 Clinical Practice Guidelines for Overweight and Obesity in Korea.
[b]Walking frequency: based on the recommended walking activity according to the physical activity guidelines in Korea.
[c]Chronic disease was defined as diagnosed diseases, such as hypertension and dyslipidemia.

dual smoking and single smoking alone were not associated with insulin resistance. The results of previous studies, which contrary to the results of this study, can be explained by differences in study participants and differences in tools to measure insulin resistance. Therefore, further studies using various indicators of insulin resistance are required among various population groups. Previous studies have shown that smoking is generally associated with the risk of insulin resistance in the general population and increases the risk of T2DM (33, 34). A possible explanation for this is that smoking directly increases the risk of insulin resistance through hormone activation and indirectly causes insulin resistance through its effect on abdominal obesity, which is mainly attributed to the nicotine absorbed during smoking (11). Another explanation is that smoking induces an increase in the levels of free fatty acids and impairs endothelial function, which can cause insulin resistance. Thus, these data indirectly support our results regarding the effects of dual cigarette smoking in our sample. However, we were unable to determine a direct link between e-cigarette smoking and insulin resistance.

In males with abdominal obesity, we found that dual smoking and single smoking increased the risk of insulin resistance and that dual smoking was associated with an almost 2-fold higher risk (reference group: nonsmokers). Previous studies have shown that smoking causes insulin resistance by inducing the accumulation of fat in the abdomen and an increase in the waist-to-hip circumference (35). We can assume that these mechanisms contribute to a significant increase in insulin resistance. In addition, both in male and female participants, the risk of insulin resistance was more than double that in dual and single smokers when they showed less healthy behavior, such as drinking alcohol or insufficient exercise frequency. This may support the results of previous studies that showed that the fatal combination of alcohol consumption and smoking causes serious metabolic abnormalities, that the lack of adequate physical activity significantly increases the body's visceral fat, and that combining alcohol consumption with smoking synergizes and strengthens these associations (36, 37).

This study has some limitations. First, because this is a cross-sectional study, a causal relationship between smoking behavior and insulin resistance could not be inferred. Second, the type of e-cigarette, frequency of vaping, and nicotine concentration could not be considered because of data limitations. Third, in the KNHANES data, data on smoking behavior, health behavior, and socioeconomic status may have been underestimated or overestimated because data were collected through self-report surveys, and some survey questions may be subject to recall bias. Moreover, given the negative social attitude toward female smokers in Korea, female respondents often misreport their actual smoking status, and thus, additional bias may have been introduced in the self-report survey (38). Fourth, in our study, participants with T2DM were excluded to rule out possible confounding factors that could affect insulin resistance. Although this approach may have ruled out other possible confounding factors that may affect insulin resistance, such exclusion may have underestimated the association between smoking behavior and insulin resistance. Fifth, we were not able to provide a sufficient discussion on dual smoking because there have been an insufficient number of studies on the relationship between dual smoking and insulin resistance. Lastly, the number of participants who used only e-cigarettes was so small that it was not possible to consider this group separately. Therefore, future studies should consider each smoking behavior separately.

However, despite these limitations, our research has several advantages. First, the analyzed data were collected from a national survey based on random cluster sampling, and our results reflect the general health status of the Korean population. Second, unlike previous studies that examined insulin resistance using HOMA-IR (20, 32), we used the TyG index with high predictive power to evaluate insulin resistance to investigate the relationship between smoking patterns and insulin resistance in Korean adults. According to previous studies, the TyG index was a better indicator for predicting T2DM than the visceral adiposity index, lipid accumulation product, and HOMA-IR (39). Third, the TyG index was measured through clinical testing; hence, it was based on more reliable and clear data. Fourth, few other studies have evaluated the association between smoking behavior, including the use of e-cigarettes, and insulin resistance. Thus, our results may provide evidence for future studies investigating an association between smoking behaviors, especially dual smoking, and insulin resistance.

In conclusion, our results have public health significance because this study provides insights on preventing T2DM, a high-burden disease, by investigating the relationship between smoking behaviors and insulin resistance. Additionally, this study is one of the few to investigate the combined and individual effects of cigarettes and e-cigarettes on insulin resistance. We found that dual smoking (cigarettes and e-cigarettes) was negatively related to insulin resistance. This suggests that the rate of insulin resistance could be lowered if doctors and the general population were educated about the adverse effects of dual smoking. However, our results do not clarify the health effects of e-cigarette use alone. Therefore, future studies should specifically investigate the negative effects of e-cigarette use on health.

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