Association between Smoking Behavior and Insulin Resistance Using Triglyceride-Glucose Index among South Korean adults

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INTRODUCTION

- Insulin resistance is defined as an attenuated biological response produced by normal or elevated insulin levels. Furthermore, insulin resistance is a fundamental aspect of T2DM and is also related to various pathological and physiological aftereffects, including hyperlipidemia, hypertension, and cardiovascular disease.
- Because insulin tests are not readily available and are expensive in most developing countries, the triglyceride-glucose (TyG) index, which can be determined using a simple blood test, is a useful indicator of blood sugar and triglyceride levels in diabetes patients.
- One of the lifestyle factors that can directly or indirectly affect insulin resistance is smoking. Electronic cigarettes (e-cigarettes) were introduced in Korea in 2007 as a healthy alternative to cigarettes or as a smoking cessation aid. However, most e-cigarette users do not stop smoking but rather use both e-cigarettes and conventional cigarettes (dual smokers).
- Research on the long-term toxicity of e-cigarettes is limited, and the results of studies showing that e-cigarettes are a healthier alternative to conventional cigarettes are mixed. Also, although the health effects of dual smoking on health are still unknown, dual smoking is likely to lead to tobacco dependence, and there is insufficient evidence to clarify the relationship between dual 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 source**: 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.
- **Study population**: This study was carried out on data derived from the KNHANES on 11,653(4721 males and 6932 females) respondents aged ≥19 years after exclusion of those with missing values.
- **Outcome variables**: The outcome variable TyG index is calculated using the formula ln[triglyceride (mg/dL) × fasting blood glucose (mg/dL)/2] and is expressed on a logarithmic scale. 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).
- **Interesting variables**: The Interesting variable was the smoking behavior of participants who used both conventional and e-cigarettes. In the KNHANES survey, all subjects were asked whether they currently use conventional or e-cigarettes or whether they have been using these products for a long time or in the past. Based on this, we categorized our subjects in to four categories: dual smokers (both conventional and e-cigarettes), single smokers (only conventional cigarettes), ex-smokers (previous smokers), and non-smokers.
- **Covariates:** Control variables that can act as potential confounding variables include socioeconomic, health-related factors and survey year. 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**: 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. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC, USA). A $p < 0.05$ was considered statistically significant.

RESULTS

Table 1. General characteristics of the study population

Variables	Total		Triglycerides and glucose(TYG)								
			Male					Female			
			Low (<8.5)		High(≥8.5)		*P*-value	Low (<8.5)		High(≥8.5)		*P*-value
	N	%	N	%	N	%		N	%	N	%	
Total	11,653	100.0	1,744	15.0	2,977	25.55		4,232	36.3	2,700	23.17	
Smoking Behavior							<.0001					0.0066
Dual smoker	197	1.7	40	2.3	124	4.2		19	0.4	14	0.5	
Single smoker	1,736	14.9	427	24.5	1,001	33.6		160	3.8	148	5.5	
Ex-smoker	2,312	19.8	703	40.3	1,189	39.9		267	6.3	153	5.7	
Non-smoker	7,408	63.6	574	32.9	663	22.3		3,786	89.5	2,385	88.3	

- In Table1, the total 11,653 participants, 4,721 were male (40.5%) and 6,932 were female (59.5%). Of the 4,721 males, 164 (3.5%) were dual-smokers, 1,428 (30.2%) were single-smokers, 1,892 were ex-smokers (40.1%), and 1,237 (26.2%) were non-smokers. Of the 6,932 females, 33 (0.5%) were dual-smokers, 308 (4.4%) were single-smokers, 420 were ex-smokers (6.1%), and 6,171 (89.0%) were non-smokers.

Table 2. Association between smoking behavior patterns and Triglycerides and glucose(TYG) index

Variables	Triglycerides and glucose index (over 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)
Non-smoker	1.00			1.00		

- In Table2, among the male participants, compared with non-smokers, 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 non-smokers, 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.

RESULTS

Table 3. Subgroup analysis stratified by independent variables

Variables	Triglycerides and 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)

[a] BMI : Body mass index/obesity status defined by BMI based on the 2018 Clinical Practice Guidelines for Overweight and Obesity in Korea.
[b] Walking frequency: Based on the recommended walking volume according to the physical activity guidelines in Korea.
[c] Chronic disease was defined as diagnosed diseases: hypertension, dyslipidemia

- In Table 3, we found that both male and female participants in the dual-smoker group and single-smoker group who consumed alcohol (male, dual: OR=2.34, single: OR=1.73; female, dual: OR=2.32, single: OR=1.78) and walked infrequently (male, dual: OR=2.19, single: OR=2.01; female, dual: OR=3.26, single: OR=1.64) had a high risk of insulin resistance
- For men with chronic disease, there was an increased risk of insulin resistance in the dual smoker and single smoker groups and was also statistically significant (male, dual: OR=2.14, single: OR=1.70).
- 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, single: OR=2.25); female dual-smokers and single-smokers in the underweight/normal weight group had the highest risk of insulin resistance (dual: OR=3.65, single: OR=1.62).
- 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 non-smoker group as reference (dual: OR=2.34, single: OR=1.73).

DISCUSSION

- This study 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.
- A possible explanation for this is that smoking directly increases the risk of insulin resistance through hormone activation and indirectly causes insulin resistance due to its effect on abdominal obesity, which is mainly attributed to the nicotine absorbed during smoking. 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.
- Additionally, In males with abdominal obesity, we found that dual smoking was associated with an almost 2-fold higher risk of insulin resistance. 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. Furthermore, in both 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, i.e., 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.
- There were several limitations in our study. First, we used cross-sectional data for this study. Therefore, causality and directionality of the observed relationship could not be established. Second, for the KNHANES data used in this study, data on smoking behavior and socioeconomic and health-related variables may have been over or underestimated because the survey was collected through self-reporting, and some surveys may have a recall bias. Third, the number of participants who only used e-cigarettes was so small that it was not possible to consider this group separately. Therefore, future studies should consider each smoking behavior separately.
- Despite these limitations, our research has several strengths. First, the analyzed data were collected from a national survey based on random cluster sampling, and our results can reflect the general health status of the Korean population. Second, 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. Third, the TyG index was measured through clinical testing; hence, it was based on more reliable and clear data.

CONCLUSION

- This study findings suggested that smoking behaviors such as conventional cigarette smoking and dual smoking are negatively affected health in adults in South Korea. Therefore, the implication of our findings can help develop interventions and policies to prevent the adverse health effects of dual smoking.
- However, it is not clear whether the independent use of e-cigarettes is associated with Insulin Resistance or affects other health outcomes. Hence, further research specifically investigating the negative effects of e-cigarettes on health and the adverse health effects of dual smoking is required.