JOMH
Journal of Men's Health

Original Article
DOI: 10.15586/jomh.v16i3.272

LONGITUDINAL STUDY ON THE RELATIVE RISK OF TYPE 2 DIABETES MELLITUS ACCORDING TO OBESITY AND PHYSICAL ACTIVITY

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Submitted: 7 May 2020. Accepted: 27 June 2020. Published: 16 July 2020.

ABSTRACT

Background and Purpose

Diabetes mellitus is a major cause of death and can lead to complications of cardiovascular disease. High physical activity (HPA) and normal weight play a role in reducing the risk of diabetes. This study analyzed the relative risk (RR) of diabetes according to obesity and physical activity using national health census data.

Methods

Nationwide health screening was performed for all adults every 2 years. Data from 5,590,120 men and 4,102,523 women, who were followed up for 10 years, were analyzed. Physical activity questionnaires about weekly exercise frequency were used to define low physical activity (LPA, 0–2 days), moderate physical activity (MPA, 3–5 days), and high physical activity (HPA, 6–7 days). Body mass index (BMI) ≤24.9 kg/m^2 was defined as normal, BMI 25.0–29.9 kg/m^2 was overweight, and BMI ≥30.0 kg/m^2 was obese. The RR was calculated using Cox analysis.

Results

Diabetes incidence rates were 14.8% in overweight men, 20.0% in men with obesity, 17.9% in overweight women, and 22.7% in women with obesity. The RR increased by 2.5 times in men with obesity and 3.4 times in women with obesity as compared with that of individuals with a normal BMI. Among overweight and obese individuals, those with HPA had decreased risks of developing diabetes compared with those with LPA (adjusted relative risk [ARR] for overweight individuals: 0.976 for men and 0.966 for women; ARR for individuals with obesity: 0.936 for men and 0.931 for women).

Conclusion
A high BMI increases the risk of diabetes; however, as physical activity increases, the risk of diabetes decreases. In the overweight and obese groups, those with higher physical activity had a lower risk of developing diabetes.

Key words: *body mass index; diabetes mellitus; obesity; physical activity; relative risk*

INTRODUCTION

Type 2 diabetes mellitus (DM) is a condition in which hyperglycemia is caused either by impairment in insulin secretion or defects in insulin action. DM should be carefully managed because it can lead to complications such as kidney, retinal, and erectile dysfunction and vascular damage.[1, 2] Despite the ongoing study of DM, the incidence of DM continues to increase worldwide. According to a U.S. national report, the rate of DM in the U.S. was 9.5% in those over 18 between 1999 and 2002, but it gradually increased to 12.0% in 2013–2016 and 13% in 2018.[3] This is similar to rates of increase in Asian countries. In Korea, the incidence of DM in the adult population has increased from 9.5% in 2007 to 10.4% in 2018.[4] The most common causes of DM include uncorrectable factors such as genetics and age and modifiable factors such as obesity, physical activity (PA), and diet.[1, 5] Many studies focus on these modifiable factors because they can be more readily altered.

PA plays a role in improving and preventing DM. PA is recommended both for prevention and reduction in severity of the disease because it lowers insulin sensitivity and resistance and improves the elasticity of blood vessels.[6, 7] One study found that people with high PA have a decreased DM relative risk (RR) by 0.65 compared with those with low total PA.[8] Another study reported that higher levels of activity could lower the risk of DM by 0.722 compared with lower levels of activity.[9] In addition, the prevalence of DM among people with obesity was 1.43 times higher than that among overweight individuals and 2.17 times higher than that among individuals with a normal weight.[10] However, most of these studies were conducted as sample studies and are therefore subject to a group's specificity. Despite the high increase in diabetes incidence in Korea, large studies with long-term follow-up where obesity and PA are considered simultaneously are very rare.

Therefore, the purpose of this study was to analyze the RR of diabetes according to the level of obesity and PA. We hypothesized that people with a high frequency of PA would have a lower risk of diabetes and that the risk of diabetes in individuals with obesity would be higher than that in those with a normal weight. To test this hypothesis, this study used the Korean National Health Insurance Service (KNHIS) national examination screening census database for adults. More than 9 million adults without diabetes were followed up for about 10 years to analyze the RR of diabetes according to PA and body mass index (BMI).

METHODS

Research Subjects and Study Design

The database had 11,038,772 men and 8,025,787 women who received national health examinations between 2002 and 2005. Among them, 5,590,120 men and 4,102,523 women who had not been previously diagnosed with DM were included in the analysis. All included patients were followed up until 2013. During the follow-up period, patients with disease codes relating to DM and those with international classification of diseases 10 codes E11–E14 were considered as having DM.[11] The participants' ages ranged from 20 to 79 years. The World Health Organization criteria for BMI were used: normal weight (18.5 to <25.0 kg/m^2), overweight (25.0 to <30.0 kg/m^2), and obese (≥30.0 kg/m^2).[12] This study was supported by the KNHIS, and the results were cited as part of a service report.[13] This study was conducted with IRB approval (Yonsei University Gangnam Severance Hospital, 3-2015-0059).

Health Screening and Health Questionnaire

Health screening include health-related questionnaires, blood tests, urine tests, body measurements, blood pressure, electrocardiography, chest radiography, and endoscopy. Subjects were asked to fast for 8 h prior to testing.

The health-related questionnaires included questions about past or recent disease information such as surgical history and medical history. Furthermore, PA, smoking, and alcohol consumption habits were investigated. The PA questionnaire asked how frequently the individual exercises each week as "How many times a week do you sweat during exercise?" The American College of Sports Medicine (ACSM) guidelines recommend at least 3 days of high-intensity activity and at least 5 days of medium-intensity activity.[14] PA was therefore classified as low physical activity (LPA, 0–2 days per week), moderate physical activity (MPA, 3–4 days per week), or high physical activity (HPA, 5–7 days per week).

The survey included information on smoking, alcohol consumption, and household income, which were the correction variables. The questionnaire asked whether the individual currently smoked or had ever smoked. Using the type, frequency, and amount of alcohol an individual consumed, the pure alcohol amount was calculated according to the WHO classification criteria, and patients were classified to be at low risk (1–40 g/day), medium risk (41–60 g/day), or high risk (more than 61 g/day).[15]

Data Analysis

The SAS (version 9.4; SAS Institute Inc. Cary, NC, USA) statistical package was used for analysis. Age, height, weight, BMI, total cholesterol (TC), aspartate transaminase (AST), alanine transaminase, and glucose were recorded as means and standard deviations; one-way ANOVA was then performed. Cox regression analysis was performed for RR according to PA and BMI. The adjusted relative risk (ARR) values with age, alcohol consumption, smoking, and household income were calculated. Statistical significance was set at $p<0.05$.

RESULTS

General Characteristics

Tables 1 and 2 display the general characteristics of the subjects. Among men, 82.1% had LPA, 10.7% had MPA, and 7.2% had HPA, whereas 84.9%, 8.1%, and 7.0% of women had LPA, MPA, and HPA, respectively. For men, the HPA group was the oldest (49.0±14.5 years), whereas among women, the LPA group was the oldest (52.2±12.6 years). The BMI was the lowest in the HPA group for both men and women, and in the HPA groups, the proportions of men and women with normal BMIs were 82.1% and 74.3%, respectively ($p<0.001$). For women, all the variables were significantly different between the PA groups. For men, there was no significant difference in TC and AST, but the differences between the groups in all other variables were significant. Both men and women with LPA were more likely to smoke than those with MPA or HPA (50.4% and 3.4%, respectively). For men and women, the HPA group had a high normal BMI and low current smoking rate ($p<0.001$).

TABLE 1 Characteristics of Subjects

	LPA	MPA	HPA	p-value
Men (N=5,590,120)	4,588,446 (82.1%)	599,116 (10.7%)	402,559 (7.2%)	
Age, year	43.0±13.2	42.7±12.3	49.0±14.5	<0.001*
Height, cm	168.5±6.2	170.1±5.9	169.4±6.2	<0.001*
Weight, kg	68.6±9.7	70.4±9.6	68.4±10.1	<0.001*
BMI, kg/m^2	24.5±3.2	24.2±2.0	23.8±1.6	<0.001*
Total cholesterol, mg/dl	193.9±48.2	194.7±47.1	193.6±49.0	NS
Fasting glucose, mg/dl	96.2±31.2	95.9±30.5	99.1±34.7	<0.001*
AST, mg/dl	28.2±22.2	27.8±22.7	28.6±23.8	NS
ALT, mg/dl	30.9±29.6	29.5±28.7	28.3±26.6	<0.001*
Women (N=4,102,523)	3,481,057 (84.9%)	334,302 (8.1%)	287,164 (7.0%)	
Age, year	52.2±12.6	45.8±12.6	45.7±15.2	<0.001*
Height, cm	155.2±5.8	157.0±5.6	156.0±6.3	<0.001*
Weight, kg	57.7±7.9	57.4±7.6	55.9±8.2	<0.001*
BMI, kg/m^2	24.0±2.8	23.3±2.1	23.0±1.9	<0.001*
Total cholesterol, mg/dl	193.6±51.6	195.4±49.5	201.2±53.5	<0.001*
Fasting glucose, mg/dl	93.1±28.2	92.6±26.0	96.5±32.1	<0.001*
AST, mg/dl	22.8±18.7	22.9±14.5	24.2±21.1	<0.001*
ALT, mg/dl	19.5±21.3	19.6±19.5	20.9±20.0	<0.001*

LPA, low physical activity; MPA, moderate physical activity; HPA, high physical activity; BMI, body mass, index; AST, aspartate transaminase; ALT, alanine transaminase.
**p<0.05.*

Diabetes Incidence and RR According to BMI

Table 3 shows the incidence of DM according to BMI. The incidences of DM were 9.3% in men who were of normal weight, 14.8% in overweight men, and 20.0% in men with obesity. The incidences of DM were 8.8% in women who were of normal weight, 17.9% in overweight women, and 22.7% in women with obesity. The ARR with the correction variable applied for overweight men increased to 1.518 (95% CI, 1.329–1.724) that of men who were normal weight, and that for men with obesity was 2.544 (95% CI, 2.241–2.716). The ARR for women who were overweight increased by 2.118 (95% CI, 1.910–2.409) times that of women who were normal weight, and that for women with obesity increased by 3.466 (95% CI, 3.001–3.820).

RR of Diabetes Due to Obesity and PA

Table 4 shows the ARR of DM. Among overweight men, the ARR significantly decreased to 0.964 (95% CI, 0.953–0.974; p<0.001) and 0.976 (95% CI, 0.963–0.988; p<0.001) in the MPA and HPA groups, respectively. Among men with obesity, the RR did not decrease in the MPA group, but it was lower in the HPA group (ARR, 0.936; 95% CI, 0.899–0.975; p<0.001). Among women, the ARR was significantly lower in the overweight HPA group (ARR, 0.966; 95% CI, 0.957–0.975; p<0.001) than in the overweight LPA group, and it was reduced to 0.931 (95% CI, 0.914–0.947; p<0.001) in the obesity group. However, among participants with normal body weight, HPA showed an inverse relationship with ARR for DM in both men and women.

TABLE 2 Body Mass Index, Smoking and Alcohol Habit of Subjects

	LPA	MPA	HPA	p-value
Men				
BMI (%)				<0.001*
Normal	79.2	80.7	82.1	
Overweight	12.1	11.5	10.0	
Obesity	8.7	7.8	7.9	
Smoking present (%)				<0.001*
Never	36.1	38.1	42.1	
Quit smoking	13.5	19.4	18.0	
Now smoker	50.4	42.5	40.0	
Alcohol habit (%)				<0.001*
None	55.3	53.5	52.2	
Low risk	28.9	26.1	32.8	
Medium risk	10.5	12.0	11.7	
High risk	5.3	8.4	3.3	
Women				
BMI (%)				<0.001*
Normal	66.3	74.0	74.3	
Overweight	30.2	23.5	22.7	
Obesity	3.5	2.5	3.0	
Smoking status (%)				<0.001*
Never	95.0	95.8	95.7	
Quit smoking	1.6	1.2	1.6	
Now smoker	3.4	3.0	2.7	
Alcohol habit (%)				<0.001*
None	89.2	90.2	90.3	
Low risk	8.0	7.2	6.5	
Medium risk	0.7	0.6	0.7	
High risk	0.1	0.1	0.2	

LPA, low physical activity; MPA, moderate physical activity; HPA, high physical activity; BMI, body mass, index. BMI normal, 18.5–24.9; overweight, 25.0–29.9; obesity, 30.0 or more. Alcohol low risk, 1–40 g/day; medium risk 41–60 g/day; high risk, 61 g/day.
**p<0.05.*

TABLE 3 Diabetes Incidence Rate and Adjusted Relative Risk According to Body Mass Index

Group	Men			Women		
	Non-DM	DM	ARR (95% CI)	Non-DM	DM	ARR (95% CI)
Normal	90.7%	9.3%	Reference	91.3%	8.8%	Reference
Overweight	85.2%	14.8%	1.518 (1.329–1.724)*	85.1%	17.9%	2.118 (1.910–2.409)*
Obesity	80.0%	20.0%	2.544 (2.241–2.716)*	77.3%	22.7%	3.466 (3.001–3.820)*
p-value	<0.001*		<0.001*	<0.001*		<0.001*

ARR; Adjusted relative risk; DM, diabetes mellitus; CI, confidence interval.
**p<0.05. Adjusted age, smoking, alcohol, family income.*

TABLE 4 Diabetes Relative Risk According to Body Mass Index and Physical Activity

Group		Men		Women	
BMI	PA level	ARR (95% CI)	p-value	ARR (95% CI)	p-value
Normal	LPA	Reference	–	Reference	–
	MPA	1.012 (1.001–1.022)	0.024*	0.967 (0.954–0.979)	<0.001*
	HPA	1.005 (0.994–1.017)	0.308	1.016 (1.004–1.029)	0.009*
Overweight	LPA	Reference	–	Reference	–
	MPA	0.964 (0.953–0.974)	<0.001*	0.930 (0.921–0.939)	<0.001*
	HPA	0.976 (0.963–0.988)	<0.001*	0.966 (0.957–0.975)	<0.001*
Obesity	LPA	Reference	–	Reference	–
	MPA	0.987 (0.955–1.020)	0.451	0.900 (0.883–0.918)	<0.001*
	HPA	0.936 (0.899–0.975)	<0.001*	0.931 (0.914–0.948)	<0.001*

ARR; Adjusted relative risk; PA, physical activity; BMI, body mass index; LPA, low physical activity; MPA, moderate physical activity; HPA, high physical activity; CI, confidence interval.
$^*p<0.05$. Adjusted age, smoking, alcohol, family income.

DISCUSSION

DM was the sixth most common cause of death in Korea in 2018, accounting for 17.1 deaths in 100,000 people.[16] DM can also lead to complications such as retinopathy, peripheral artery and cardiovascular risk, and kidney disease.[1] Even without taking into account these other complications, DM increases the mortality and morbidity of vascular disease. In a previous study of 13,000 people with a 20-year follow-up, patients with diabetes had a 2- to 3-fold increase in the risk of myocardial infarction or stroke and a 2-fold increase in mortality risk.[17] In addition, DM is a representative cardiovascular risk inducer and is also a risk factor of hypertension and hyperlipidemia.[18] Obesity and inactivity are typical risk factors for DM that should be managed seriously. Obesity increases insulin demand and damages insulin metabolism.[19] PA is considered an effective, non-pharmacological method to manage cardiovascular disease and risk factors by improving obesity, insulin sensitivity, and elasticity of blood vessels.[6] Therefore, this study used the nationwide census survey conducted in all regions of Korea to analyze the incidence of DM according to obesity and PA. The subjects were adult men and women who did not have DM at the start of the study.

The main result of this study was that the RR of DM decreased as PA increased (Table 4). Among overweight and obese men and women, those with HPA had a reduced risk of DM compared with those with LPA. In particular, the risk of developing DM among men with obesity decreased by 6.4%, and the risk among women with obesity decreased by 10.0%. In a similar study that followed up participants for 10 years, active individuals had a 51% lower risk of developing DM than inactive individuals.[20] Although the effectiveness of PA for reducing DM risk was lower in this study than in previous studies, most studies agree that increasing PA is a key solution.[21, 22] However, participation in PA is relatively low. One study found that 27.5% of people worldwide had insufficient PA.[23] In our study, only 10.7% and 7.2% of men had moderate and high activity, respectively, and only 8.1% and 7.0% of women had moderate and high activity, respectively. However, the questionnaire is based on the premise that the intensity of activity required for sweating requires a higher intensity activity than walking. Even so, these results indicate a low participation rate in PA. Therefore, national and individual efforts to increase PA must be made simultaneously. According to one survey, people do not exercise because of lack of time, concerns about affordability, and poor health.[24] Therefore, the state should pay attention to supporting exercise facilities and creating accessible environments, as this can help individuals develop the important habit of participating in PA, even for a short time. The ACSM also recommends an intermittent exercise method.[14] According to a study by Trapp et al.,[25] 15 weeks of intermittent exercise led to significant body fat loss.

Economic growth is associated with decreased PA. The proportions of physical inactivity are 16.2% in low-income countries and 36.8% in high-income countries.[23] This is because people in countries with a high economic level often have a low level of professional or mobility activities that must be carried out, even if they do a lot of selective recreational PA. In the past 50 years, daily energy consumption among U.S. individuals has been reduced by more than 100 kcal.[26] Individuals in Asian countries, including Korea, may have less activity due to economic growth and also may have increased consumption of high-calorie foods, leading to an increase in obesity.[27–29]

Unlike most previous studies, our study showed controversial results. Among men with a normal BMI, MPA increased the RR of DM significantly by 1.012, whereas among women with a normal BMI, HPA increased the RR of DM by 1.016. This type of result should be interpreted with caution. Burke et al.[30] also found similar results; in their study, participants who exercised more than once a week showed a 1.19-fold increase in DM incidence compared with inactive participants. Although not significant, the study by Chien et al.[31] also showed a 1.24-fold increase in DM incidence in people with high leisure activity. PA includes leisure, sports, exercise, labor, and daily activities. These studies may be limited in their analysis because only exercise was investigated. The absence of nutrition and lifestyle information may also have influenced the results. DM is heavily influenced by obesity, and the fact that this was not investigated is also a limitation of this study.

Another important result of this study is that the RR of diabetes increased with obesity, regardless of PA. In this study, the incidence of disease increased linearly as obesity increased, which is similar to the results of many other studies. The incidence of DM increased by 20% in men and 22% in women. In addition, it increased 1.5 times in overweight men, 2.5 times in men with obesity, 2.1 times in overweight women, and 3.4 times in women with obesity when compared with individuals with a normal BMI. Some studies have uncovered an obesity paradox wherein obesity is not always dangerous.[32] However, even more studies highlight the risk of obesity. In previous studies, those who were overweight were 1.43 times more likely to develop DM than those who were of normal weight, and individuals with obesity had a 2.17-times increased prevalence of diabetes.[10] In other studies, the incidence increased 3.22 times in overweight individuals and 9.06 times in individuals with obesity.[33, 34]

Although this study reported significant results using BMI, numerous studies have reported a significant association between cardiovascular disease factors and waist circumference.[35] Therefore, longitudinal studies using various variables to diagnose obesity are needed. Although our results are similar to those of previous studies, the incidence of DM in women was higher than that previously observed. Most previous studies report a high incidence of DM in men. A follow-up study of Chinese subjects showed that men had a 1.26-times higher prevalence of DM than women.[10] In a study of Korean individuals, the incidence of diabetes among men was 12.9%, whereas it was 7.9% among women, indicating that men were 1.6 times more likely than women to have diabetes.[4] As our population was similar to that of this previous study, our study may have differed in terms of initial sample recruitment and measurement year. Additionally, DM is the 7th highest cause of death for Korean men but the 6th highest for women.[16] Furthermore, outcomes may differ in the elderly population.

Finally, the higher the PA, the healthier an individual is. Individuals with HPA had the highest probability of having normal weight; likewise, people with HPA had a higher rate of smoking cessation and non-smoking, and men with HPA had lower alcohol consumption. These results are consistent with findings regarding a holistic health care linkage.[36]

This study was conducted using nationwide census data, and despite it being a rare large-sample study with long-term follow-up, it has some limitations. It does not include the family history, nutrition, or lifestyle surveys described above. In addition, although participation and non-participation in exercise may vary from year to year, various changes occurring during the follow-up period were not reflected in this analysis.

In particular, diabetes is a representative senile disease, and the elderly have various comorbidities. Therefore, the health care model emphasizes that government agencies' public health policies and social support should be considered.[37] Future studies will also need to be extensively conducted on the causality and linkages of other diseases related to diabetes and the effectiveness of policies. Furthermore, it will require more advanced methods to supplement these points, and further studies on the prevention of complications through post-diabetes tracking as well as PA will lead to better treatment of DM.

CONCLUSION

Individuals with obesity are more likely to develop DM; however, a higher frequency of PA decreases the risk of diabetes. In particular, the positive effect of PA was better in the overweight and obese groups, and there were conflicting results in the normal weight group. Men and women with obesity had an increased risk of diabetes by 2.5 times and 3.4 times, respectively, compared with their respective normal weight counterparts. However, even in the obesity group, the risk of developing diabetes decreased by about 6.4% in men and about 10.0% in women when participating in HPA.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research was supported by the KNHIS research fund and service in 2015.

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