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# Association between breakfast frequency and insulin resistance in Korean adults with prediabetes: A nationwide population-based cross-sectional study



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#### ABSTRACT

*Aims*: This study aimed to investigate the association between breakfast frequency and insulin resistance using the triglyceride and glucose (TyG) index in Korean adults with prediabetes.

*Methods*: This study used data from the 2016–2018 Korea National Health and Nutrition Examination Survey (KNHANES). A total of 16,925 participants were included in this study. Breakfast frequency was classified as 0 times, 1-4 times, and 5-7 times per week. High insulin resistance was defined as a TyG index of  $\geq$ 8.5. A multivariate logistic regression analysis was performed.

*Results:* Compared with the group whose breakfast frequency was 5–7 times per week, the odds ratio for high insulin resistance was 1.39 times (95% confidence interval (CI), 1.21–1.59) and 1.17 times (95% CI, 1.04–1.32) higher in the group whose breakfast frequency was 0 times and 1–4 times per week, respectively.

Conclusions: This study revealed that a lower frequency of breakfast consumption was significantly associated with a higher risk of insulin resistance in Korean adults with prediabetes. In the future, a large-scale prospective longitudinal study is required to establish the causal relationship between breakfast frequency and insulin resistance.

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#### 1. Introduction

Prediabetes refers to the stage of dysglycemia between normoglycemia and type 2 diabetes mellitus (DM) [1]. Prediabetes is defined as the presence of at least one of the following three categories: 1) HbA1c between 5.7% and 6.4%; 2) impaired glucose tolerance, defined as a blood glucose level of 140–199 mg/dL 2 h after the 75 g oral glucose tolerance test [2]; and 3) impaired fasting blood glucose, defined as a fasting blood glucose level between 100 mg/dL and 125 mg/dL [3]. Prediabetes is a condition with a high risk of progression to diabetes, with a yearly progression rate of

5–10% [4]. In 2019, the International Diabetes Federation reported that the estimated worldwide prevalence of impaired glucose tolerance is 7.5% [5]. Between 2015 and 2016, the prevalence of prediabetes was 43.5% in adults 20 years old or older [6]. In Korea, from 2007 to 2017, the prevalence of impaired fasting glucose among adults aged 30 or older increased from 20.2% to 26.3% [7]. Moreover, several studies have reported that prediabetes is related to health problems, such as morbidity and mortality, and increased financial burden [8–13].

Insulin resistance is a major pathophysiological mechanism of prediabetes and type 2 DM [14,15], and several studies have reported an association between skipping breakfast and insulin resistance [16–20]. To identify insulin resistance, the TyG index is commonly used. TyG index is calculated using fasting blood triglyceride level and fasting blood glucose level, and it has a high sensitivity for identifying insulin resistance [21].

In a cross-sectional study that studied the association between breakfast frequency and insulin resistance using the TyG index in adults without diabetes using data collected between 2016 and

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Abbreviations: BMI, body mass index; CI, confidence interval; HbA1c, glycated hemoglobin; KNHANES, Korea National Health and Nutrition Examination Survey; OR, odds ratio; TyG index, triglyceride and glucose index.

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2018 from the KNHANES, the odds ratio for insulin resistance was 1.17 and 1.42 for the group with an average breakfast frequency of 1–4 per week and 0 per week respectively, compared to the group with an average breakfast frequency of 5–7 per week [16]. Furthermore, in a randomized crossover study that examined the association between skipping breakfast and 24-h energy expenditure and 24-h blood glucose level in Japanese males in their 20s, skipping breakfast increased the 24-h average blood glucose [18].

The potential mechanisms that highlight the association of frequent breakfast skipping with a higher risk of insulin resistance include that 1) breakfast skipping disrupts the circadian rhythm [22], which has been closely associated with the pathophysiology of type 2 diabetes [23], and 2) by skipping breakfast, the absence of glucose elevation due to fasting until noon may diminish  $\beta$ -cell responsiveness and memory, leading to a reduced and delayed insulin response after lunch [22], whereas the magnitude of insulin release is enhanced significantly by previous glucose exposure [24].

However, these prior studies were limited to the general population, and to our knowledge, no study has investigated the association between breakfast frequency and insulin resistance only in people with prediabetes, who are more likely to progress to diabetes. Reducing insulin resistance is important to prevent progression to diabetes in people with prediabetes and could be a method to prevent progression to diabetes.

This study aims to identify the association between breakfast frequency and insulin resistance, using the TyG index. Therefore, we hypothesized that in adults aged  $\geq$ 19 years with prediabetes, less breakfast frequency is associated with higher insulin resistance and conducted a cross-sectional study using data collected between 2016 and 2018 from the KNHANES.

#### 2. Materials and methods

#### 2.1. Subjects

This secondary data analysis assessed data collected between 2016 and 2018 from the KNHANES. The KNHANES is a nationwide population-based survey that examines the general health and nutritional status of the civilian non-institutionalized population in South Korea conducted by the Korean Ministry of Health and Welfare and the Division of Chronic Disease Surveillance of the Korean Centers for Disease Control and Prevention. Of the 24,269 people surveyed, we first excluded people under 19 years old and those who fell under any of these three categories: 1) had been diagnosed with or treated for DM; 2) HbA1c level was not between 5.7% and 6.4%; 3) fasting blood glucose level was not between 100 mg/dL and 125 mg/dL. After exclusion, among the remaining 17,535 people, those with missing TyG index, which represents insulin resistance, were excluded, and finally 16,295 people were included in the study population (Fig. 1).

Written informed consent was obtained from all participants before participating in the study, and the KNHANES was conducted with ethical approval from the Institutional Review Board of the Korea Centers for Disease Control and Prevention (KNHANES was exempt from research ethics review based on the Bioethics and Safety Act from 2016 to 2017 [25] and no. 2018-01-03-P-A in 2018).

#### 2.2. Data collection

Participants were interviewed by trained staff using standardized health questionnaires to collect data on demographic information, medical history, lifestyle, and nutrient intake [25]. Anthropometric measurements and laboratory tests were also performed. The independent variable, the frequency of breakfast, was assessed using the KHNAES VII questionnaire; the frequency of

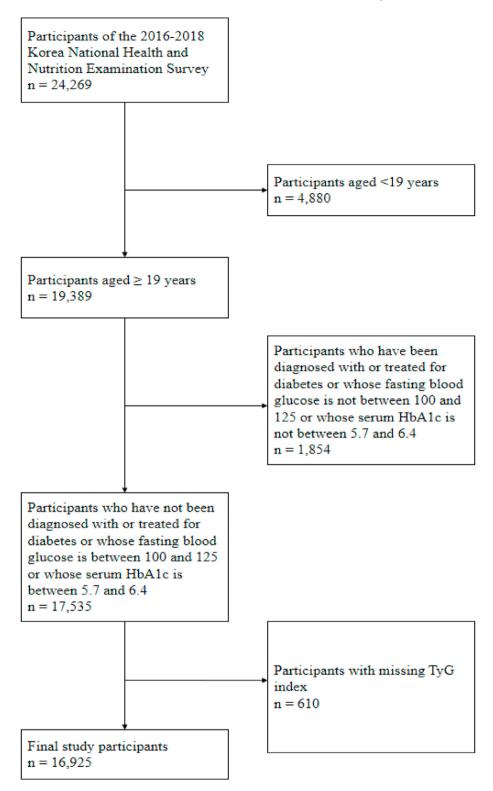
breakfast for 1 week over the past year was expressed in three categories (0 per week, 1–4 per week, 5–7 per week). Furthermore, variables such as age, sex, income level, education level, marital status, residential area, occupation, smoking, alcohol intake, physical activity, obesity, weekly lunch frequency during the past year, weekly dinner frequency during the past year, daily energy intake, average daily carbohydrate intake, average daily protein intake, and average daily fat intake were adjusted. The income level was expressed in four categories: low, medium-low, medium-high, and high. Level of education was expressed in two categories: "under high school graduate" and "high school graduate or higher." Marital status was classified into three categories: "single," "married," and "divorced or widowed." Residential areas were divided into two categories: "urban" and "rural," with "Seoul," "Busan," "Daegu," "Incheon," "Gwangju," "Daejeon," "Ulsan," "Sejong," "Gyeonggi" being classified as "urban" areas and "Gangwon," "Chungbuk," "Chungnam," "Jeonbuk," "Jeonnam," "Gyeongbuk," "Gyeongnam," and "Jeju" classified as "rural" areas. The occupation was expressed in four categories: "office worker," "service worker," "skilled worker," and "unemployed," and smoking status was classified into three categories: "non-smoker," "past smoker," and "current smoker." Alcohol intake was defined as drinking at least one drink per month in the last year, and physical exercise was defined as 150 min of moderate-intensity physical activity or 75 min of high-intensity physical activity, or an equivalent time of mixed moderate- and high-intensity physical activity per week. Obesity was defined as a body mass index (BMI; calculated by dividing weight [kg] by the square of height  $[m^2]$ ) of >25 kg/m<sup>2</sup>. The average frequency of lunch and dinner per week over the past year was expressed in three categories: 0 per week, 1–4 per week, and 5–7 per week. Daily energy (kcal/day), carbohydrate (g/day), protein (g/day), and fat (g/day) intakes were expressed as continuous variables. Serum triglycerides and fasting blood glucose levels were measured using an automatic analyzer (Hitachi 7600, Tokyo,

For measuring insulin resistance, the dependent variable, the TyG index, was used. The TyG index is calculated using fasting blood glucose and triglycerides and is useful for evaluating insulin resistance [26]. When comparing the two measures to evaluate insulin resistance, the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and the TyG index, studies have shown that the TyG index is better at predicting the prevalence of metabolic syndrome and type 2 DM [27,28]. The TyG index was calculated using the following equation: Ln (triglyceride (mg/dL) × fasting glucose (mg/dL)/2) [29], and insulin resistance was defined as TyG  $\geq$ 8.5. The cut-off value of the TyG index, 8.5, is a value that previous studies found to increase the risk of metabolic disorders. Zhang et al. found that a TyG index  $\geq$  8.5 or higher is extremely sensitive to the diagnosis of non-alcoholic fatty liver disease [30], and Joo et al. found a high association between a TyG index of >8.5 and insulin resistance in Korean adults without diabetes [16].

#### 2.3. Statistical analysis

The characteristics of the participants classified according to high insulin resistance using the TyG index are expressed as means and standard deviations for continuous variables and as numbers and percentages for categorical variables. The participant groups were compared using the independent *t*-test for continuous variables and the Chi-square test for categorical variables.

Multivariate logistic regression analysis was used to analyze the association between breakfast frequency and high insulin resistance using the TyG index. Relative risks were estimated using odds ratios (ORs) and 95% confidence intervals (CIs). We adjusted for multiple variables that showed significant associations in the



**Fig. 1.** Flow diagram of the selection of study participants HbA1c, glycated hemoglobin; TyG index, triglyceride and glucose index.

univariate analysis and those with clinical relevance. After calculating the crude ORs (Model 1), Model 2 was adjusted for age, sex, income, education level, occupation, residential area, marital status, smoking, alcohol intake, physical activity, and obesity. Model 3 was further adjusted for weekly lunch and dinner frequency,

calories, and macronutrients (carbohydrate, protein, and fat) intake.

All variables entered into the logistic regression analysis were examined for multicollinearity and only those with a variance inflation factor of <5 were used. All statistical analyses were

performed with SPSS version 25 (IBM, Armonk, NY, USA). The level of statistical significance was set at  $\it P < 0.05$ , and all  $\it P$ -values were two-tailed.

#### 3. Results

#### 3.1. Demographic characteristics of the participants

Table 1 shows the baseline characteristics of the study

population. The number of participants with high insulin resistance using the TyG index was 9029 (53.3% of the total). The proportion of no breakfast intake per week was higher in the high insulin resistance group than in the low insulin resistance group (P < 0.001). Regarding sex, the proportion of males in the high insulin resistance group was significantly higher (61.4%, P < 0.001). Compared with those of the low insulin resistance group, the age and the amount of daily calorie, carbohydrate, and protein intake of the high insulin resistance group were higher (P < 0.001). In addition,

**Table 1**Demographic characteristics according to insulin resistance in Korean adults with prediabetes.

Variables	Insulin resistance using the TyG index		
	Low (<8.5) (n = 7896)	High ( $\ge$ 8.5) (n = 9029)	<i>P</i> -value
Breakfast per week			<0.001
0 times	943 (15.9)	972 (16.3)	
1–4 times	1642 (26.9)	1550 (23.9)	
5–7 times	4344 (57.2)	5220 (59.8)	
Sex			< 0.001
Male	2141 (37.6)	4024 (61.4)	
Female	4789 (62.4)	3718 (38.6)	
Age	$43.27 \pm 0.29$	$49.42 \pm 0.28$	< 0.001
Marital status		<u>-</u>	< 0.001
Single	1462 (30.0)	966 (18.8)	
Married	4733 (62.1)	5603 (69.7)	
Separated or divorced	733 (7.9)	1172 (11.5)	
Income	,		0.195
Low	1654 (24.6)	1954 (24.9)	0.100
Lower-middle	1678 (23.8)	1958 (25.0)	
Upper-middle	1764 (25.5)	1935 (25.1)	
High	1819 (26.1)	1875 (25.0)	
Educational level	1013 (20.1)	1073 (23.0)	< 0.001
Middle school or lower	1572 (16.8)	2556 (25.2)	<0.001
	, ,	, ,	
High school or higher	5087 (83.2)	4846 (74.8)	.0.001
Residential region	1035 (22.5)	2404 (25.0)	<0.001
Rural	1935 (22.5)	2404 (25.8)	
Urban	4995 (77.5)	5338 (74.2)	0.404
Occupation	1050 (00.0)	4540 (00.5)	0.484
Office worker	1856 (29.9)	1710 (28.5)	
Service worker	884 (14.0)	899 (13.1)	
Manual worker	1341 (19.5)	1850 (23.8)	
Unemployed	2574 (36.6)	2936 (34.7)	
Obesity*			< 0.001
No	5465 (79.5)	4193 (53.3)	
Yes	1451 (20.5)	3521 (46.7)	
Smoking status			< 0.001
Non-smoker	4927 (68.4)	4097 (47.4)	
Past smoker	766 (13.9)	1693 (27.1)	
Current smoker	1191 (17.7)	1874 (25.5)	
Alcohol intake			< 0.001
No	3247 (42.7)	3446 (38.7)	
Yes	3638 (57.3)	4226 (61.3)	
Physical activity <sup>†</sup>			< 0.001
Inactive	3534 (48.7)	4396 (55.4)	
Active	3121 (51.3)	2995 (44.6)	
Lunch per week			0.694
0 times	106 (1.5)	156 (1.8)	
1–4 times	608 (9.3)	616 (8.0)	
5–7 times	6215 (89.2)	6970 (90.2)	
Dinner per week	, ,	, ,	0.151
0 times	31 (0.4)	32 (0.4)	
1–4 times	743 (11.6)	607 (8.6)	
5–7 times	6155 (88.0)	7103 (91.0)	
Calorie intake (kcal/day)	1964.52 ± 14.31	2117.51 ± 15.32	< 0.001
Carbohydrate intake (g/day)	291.01 ± 1.92	$307.98 \pm 1.99$	< 0.001
Protein intake (g/day)	$72.28 \pm 0.64$	$75.30 \pm 0.64$	< 0.001
		46.89 ± 0.56	0.391
Fat intake (g/day)	$47.53 \pm 0.59$	40.09 ± 0.30	0.591

TyG index, triglyceride and glucose index.

Data were obtained from the 2016–2018 Korean National Health and Nutrition Examination Survey.

The P-values were calculated using an independent t-test or a chi-square test.

Continuous variables are expressed as means and standard deviations, whereas categorical variables are expressed as numbers and percentages.

<sup>\*</sup>Defined as body mass index  $\geq$ 25 kg/m<sup>2</sup>.

<sup>†</sup>Defined as 150 min of moderate-intensity physical activity or 75 min of high-intensity physical activity, or an equivalent time of mixed moderate- and high-intensity physical activity per week.

the proportion of low education level, rural residence, obesity, current alcohol intake, and physical inactivity were also higher in the high insulin resistance group (P < 0.001).

## 3.2. Association between breakfast frequency and insulin resistance using the TyG index

Table 2 shows ORs and 95% CIs with high insulin resistance compared to the 5–7 breakfast frequency per week after dividing them into three subgroups according to breakfast frequency. The model was adjusted for age, sex, income, education level, occupation, residential area, marital status, smoking status, alcohol intake, physical activity, obesity, weekly lunch and dinner frequency, and calorie and macronutrients (carbohydrate, protein, fat) intake. The OR of insulin resistance in the group with 5–7 breakfasts per week was 1.17 (95% CI, 1.04–1.32) and 1.39 times (95% CI, 1.21–1.59) higher than that in the groups with 1–4 breakfasts and 0 breakfast, respectively.

#### 4. Discussion

In this study, it is shown that decreased breakfast frequency is associated with increased insulin resistance. As mentioned above, prediabetes is related to health problems and increased financial burden [8-13].

Although the causal relationship between breakfast frequency and insulin resistance is not identified, our study results can give a clue that frequent breakfast consumption could be a simple way of reducing the risk of prediabetes and diabetes and preventing the development of diabetes in people with prediabetes.

There have been prior studies that studied the association between breakfast consumption and insulin resistance and risk of metabolic disorders [16-20,31-34]. In a study of 14- to 18-year-old adolescents in Slovakia, skipping breakfast was identified as a significant risk factor for insulin resistance, measured using HOMA-IR [17]. A study in Japanese people without diabetes also showed that skipping breakfast, eating irregularly, and eating quickly were associated with insulin resistance, measured using HOMA-IR [19]. A randomized controlled trial of healthy lean females in the UK found that skipping breakfast impaired fasting lipid levels and postprandial insulin sensitivity [32]. A meta-analysis of studies on the Asia-Pacific population also showed a positive correlation between skipping breakfast and the prevalence of overweight and obesity [33]. A study using data from KNHANES from 2007 to 2009 found that higher breakfast energy intake was associated with lower risk of metabolic disorders [34]. These results of previous studies are consistent with the known mechanisms of insulin resistance in type 2 DM: 1) hepatic lipid accumulation activates protein kinase C and interferes with insulin signaling [35]; 2) inflammation of the liver causes Kupffer cells and macrophages to secrete proinflammatory molecules, thus decreasing insulin sensitivity [36]; 3) an unfolded protein response is induced so that it interferes with insulin signaling [37]; 4) increases in non-esterified fatty acids, glycerol, hormones, and proinflammatory cytokines, which can be observed in obese people, induce beta-cell dysfunction and promote gluconeogenesis [38]. These mechanisms also support our finding that insulin resistance increases with decreased breakfast frequency.

Compared with previous studies, this study has several differences. First, the participants were limited to people with prediabetes, who have a higher risk of progression to diabetes. People with prediabetes are more likely to progress to diabetes than the general population, and 5–10% of people with prediabetes progress to diabetes each year [4]. Second, unlike in some previous studies, the breakfast frequency in the present study was quantified and analyzed with three categories of ordinal scale: 0 times a week, 1–4 times a week, and 5–7 times a week.

#### 5. Limitation

This study has several limitations. First, this study is a crosssectional study, making it difficult to know the causal relationship; therefore, a prospective longitudinal study with a large sample is required. Second, there may have been recall bias because data about breakfast frequency were collected using a participantreported questionnaire. However, KNHANES survey interviews are conducted by well-trained staff to obtain consistent and reliable answers [39], and self-reports are common in population-based studies [40]. Furthermore, the reliability of the data and the representativeness of the entire Korean population are guaranteed, considering that the KNHANES comprises the largest source of open data in Korea and is conducted by the government. Third, in this study, the composition of the breakfast was not analyzed. In this study, the daily intake of calories and macronutrients were calculated as confounders, but the amount and the ratio of the nutrients in each meal were not analyzed; therefore, more studies on the association between insulin resistance and meal composition are required.

However, this study is the first that identified the association between breakfast frequency and insulin resistance in people with prediabetes, using nationwide data. The strength of this study is that it has added clinical significance by targeting people with prediabetes, who have a high risk of progressing to diabetes, in addition to previous studies targeting the general population. Second, the KNHANES data used in this study are large-scale and randomly sampled from the entire Korean population; therefore,

**Table 2**Unadjusted and adjusted odds ratios and 95% confidence intervals for insulin resistance using the TyG index according to weekly breakfast frequency.

Multivariate model	Model 1	Model 2	Model 3
Insulin resistance <sup>b</sup> Breakfast per week	OR (95% CI)	OR (95% CI)	OR (95% CI)
0 times	0.98 (0.87-1.10) P = 0.691	$1.41 (1.23-1.61)^a P < 0.001$	$1.39 (1.21-1.59)^a P < 0.001$
1–4 times	$0.85 (0.77 - 0.94)^a P = 0.001$	$1.17 (1.04-1.32)^a P = 0.008$	$1.17 (1.04 - 1.32)^{a} P = 0.010$
5–7 times	Reference	Reference	Reference

TyG index, triglyceride and glucose index; OR, odds ratio; CI, confidence interval. Data from the 2016–2018 Korean National Health and Nutrition Examination Survey. Model 1 is crude.

Model 2 is adjusted for age, sex, income, educational level, occupation, residential area, marital status, smoking status, alcohol intake, physical activity, and obesity.

Model 3 is adjusted for weekly lunch and dinner frequency and calorie and macronutrient intake (carbohydrate, protein, and fat) in addition to the variables adjusted in Model

a Indicates P-value <0.05</p>

<sup>&</sup>lt;sup>b</sup> Insulin resistance is defined using the TyG index, and a value greater than 8.5 is defined as insulin resistance.

the study results could be applicable to the entire Korean population. Through this, it is expected that public health benefits such as reduction of morbidity due to chronic diseases including diabetes, prevention of health problems such as complications related to diabetes, and reduction of burden of medical expenses will be achieved.

#### 6. Conclusion

In conclusion, the OR of insulin resistance was 1.17 times (95% CI, 1.04–1.32) in those with 1–4 breakfasts per week and 1.39 times (95% CI, 1.21–1.59) in those with 0 breakfast, compared to those with 5–7 breakfasts per week, among Korean adults with prediabetes. In the future, a large-scale prospective longitudinal study is required to establish the causal relationship between breakfast frequency and insulin resistance. And finally, we hope that frequent breakfast consumption would be identified as an easy and useful method for preventing the development of diabetes.

#### Availability of data and materials

The datasets analyzed during the current study are available in the [The KNHANES] repository, [https://knhanes.cdc.go.kr/knhanes/index. do]. The KNHANES is a nationwide population-based survey conducted by the Korean Ministry of Health and Welfare and the Division of Chronic Disease Surveillance of the Korean Centers for Disease Control and Prevention. All data are fully available without restriction. All data files are available from the KNHANES database.

All methods were carried out in accordance with relevant guidelines and regulations.

#### **Declaration of competing interest**

None.

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None.

#### References

- [1] American Diabetes Association; 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2020. Diabetes Care 2020;43(Supplement\_1):S14-31. https://doi.org/10.2337/dc20-S002.
- [2] National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979;28(12):1039-57. https://doi.org/10.2337/diab.28.12.1039.
- [3] Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Expert committee on the diagnosis and classification of diabetes mellitus. Follow-Up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26(11): 3160-7. https://doi.org/10.2337/diacare.26.11.3160.
- [4] Tabák AG, Herder C, Rathmann W, Brunner EJ, Kivimäki M. Prediabetes: a high-risk state for diabetes development. Lancet 2012;379(9833):2279–90. https://doi.org/10.1016/S0140-6736(12)60283-9.
- [5] Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al., IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the international diabetes federation diabetes atlas. In: Diabetes res clin pract. ninth ed., vol. 157; 2019, 107843. https://doi.org/10.1016/j.diabres.2019.107843.
- [6] Echouffo-Tcheugui JB, Selvin E. Prediabetes and what it means: the epide-miological evidence. Annu Rev Publ Health 2021;42:59–77. https://doi.org/10.1146/annurey-publhealth-090419-102644.
- [7] Shin JY. Trends in the prevalence and management of diabetes in Korea: 2007-2017. Epidemiol Health 2019;41:e2019029. https://doi.org/10.4178/ epih.e2019029.
- [8] Bloom David E, Chen Simiao, Kuhn Michael, McGovern Mark E. Les Oxley, Klaus Prettner. The economic burden of chronic diseases: estimates and projections for China, Japan, and South Korea. The Journal of the Economics of Ageing 2020;17:100163. https://doi.org/10.3386/w23601\_ISSN.2312.828X
- Ageing 2020;17:100163. https://doi.org/10.3386/w23601. ISSN 2212-828X.
  [9] Cai X, Zhang Y, Li M, Wu JH, Mai L, Li J, et al. Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-

- analysis. BMJ 2020;370:m2297. https://doi.org/10.1136/bmj.m2297.
- [10] Barr EL, Boyko EJ, Zimmet PZ, Wolfe R, Tonkin AM, Shaw JE. Continuous relationships between non-diabetic hyperglycaemia and both cardiovascular disease and all-cause mortality: the Australian Diabetes, Obesity, and Lifestyle (AusDiab) study. Diabetologia 2009;52(3):415–24. https://doi.org/10.1007/s00125-008-1246-y.
- [11] Nakagami T, DECODA Study Group. Hyperglycaemia and mortality from all causes and from cardiovascular disease in five populations of Asian origin. Diabetologia 2004;47(3):385–94. https://doi.org/10.1007/s00125-004-1334-6
- [12] Dall TM, Yang W, Gillespie K, Mocarski M, Byrne E, Cintina I, et al. The economic burden of elevated blood glucose levels in 2017: diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. Diabetes Care 2019;42(9):1661–8. https://doi.org/10.2337/dc18-1226.
- [13] American Diabetes Association. Economic costs of diabetes in the U.S. In 2017. Diabetes Care 2018;41(5):917–28. https://doi.org/10.2337/dci18-0007.
- [14] Savage DB, Petersen KF, Shulman GI. Mechanisms of insulin resistance in humans and possible links with inflammation. Hypertension 2005;45(5): 828–33 https://doi.org/10.1161/01.HYP.0000163475.04421.e4
- [15] Muoio DM, Newgard CB. Mechanisms of disease:Molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. Nat Rev Mol Cell Biol 2008;9(3):193–205. https://doi.org/10.1038/nrm2327.
- [16] Joo HJ, Kim GR, Park EC, Jang SI. Association between frequency of breakfast consumption and insulin resistance using triglyceride-glucose index: a crosssectional study of the Korea national health and nutrition examination survey (2016-2018). Int J Environ Res Publ Health 2020;17(9):3322. https://doi.org/ 10.3390/ijerph17093322.
- [17] Jurkovičová J, Hirošová K, Vondrová D, Samohýl M, Štefániková Z, Filová A, et al. The prevalence of insulin resistance and the associated risk factors in a sample of 14-18-year-old Slovak adolescents. Int J Environ Res Publ Health 2021;18(3):909. https://doi.org/10.3390/ijerph18030909.
- [18] Ogata H, Kayaba M, Tanaka Y, Yajima K, Iwayama K, Ando A, et al. Effect of skipping breakfast for 6 days on energy metabolism and diurnal rhythm of blood glucose in young healthy Japanese males. Am J Clin Nutr 2019;110(1): 41–52. https://doi.org/10.1093/ajcn/nqy346.
- [19] Shigeta H, Shigeta M, Nakazawa A, Nakamura N, Yoshikawa T. Lifestyle, obesity, and insulin resistance. Diabetes Care 2001;24(3):608. https://doi.org/ 10.2337/diacare.24.3.608.
- [20] Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. Am J Clin Nutr 2007;85(3):910–8. https://doi.org/10.1093/ajcn/85.3.910.
- [21] Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord 2008;6(4):299–304. https://doi.org/10.1089/met.2008.0034.
- [22] Jakubowicz D, Wainstein J, Landau Z, Raz I, Ahren B, Chapnik N, et al. Influences of breakfast on clock gene expression and postprandial glycemia in healthy individuals and individuals with diabetes: a randomized clinical trial. Diabetes Care 2017;40(11):1573–9. https://doi.org/10.2337/dc16-2753.
- [23] Ando H, Ushijima K, Yanagihara H, Hayashi Y, Takamura T, Kaneko S, et al. Clock gene expression in the liver and adipose tissues of non-obese type 2 diabetic Goto-Kakizaki rats. Clin Exp Hypertens 2009;31(3):201-7. https://doi.org/10.1080/10641960902822450.
- [24] Vagn Korsgaard T, Colding-Jørgensen M. Time-dependent mechanisms in beta-cell glucose sensing. J Biol Phys 2006;32(3–4):289–306. https://doi.org/ 10.1007/s10867-006-9017-9.
- [25] Korea Centers for Disease Control and Prevention. Guideline for seventh Korea national health and nutrition examination survey (KNHANES VII). Osong, Korea: Korea Centers for Disease Control and Prevention; 2016.
- [26] Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 2010;95(7):3347–51. https://doi.org/10.1210/jc.2010-0288.
- [27] Park HM, Lee HS, Lee YJ, Lee JH. The triglyceride-glucose index is a more powerful surrogate marker for predicting the prevalence and incidence of type 2 diabetes mellitus than the homeostatic model assessment of insulin resistance. Diabetes Res Clin Pract 2021;180:109042. https://doi.org/10.1016/ i.diabres.2021.109042.
- [28] Son DH, Lee HS, Lee YJ, Lee JH, Han JH. Comparison of triglyceride-glucose index and HOMA-IR for predicting prevalence and incidence of metabolic syndrome. Nutr Metabol Cardiovasc Dis 2022;32(3):596–604. https://doi.org/ 10.1016/j.numecd.2021.11.017.
- [29] Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord 2008;6(4):299–304. https://doi.org/10.1089/met.2008.0034.
- [30] Zhang S, Du T, Zhang J, Lu H, Lin X, Xie J, et al. The triglyceride and glucose index (TyG) is an effective biomarker to identify nonalcoholic fatty liver disease. Lipids Health Dis 2017;16(1):15. https://doi.org/10.1186/s12944-017-0409.6
- [31] Timlin MT, Pereira MA. Breakfast frequency and quality in the etiology of adult obesity and chronic diseases. Nutr Rev 2007;65(6 Pt 1):268–81. https:// doi.org/10.1301/nr.2007.jun.268-281.

- [32] Farshchi HR, Taylor MA, Macdonald IA. Deleterious effects of omitting breakfast on insulin sensitivity and fasting lipid profiles in healthy lean women. Am J Clin Nutr 2005;81(2):388–96. https://doi.org/10.1093/ajcn.81.2.388.
- [33] Horikawa C, Kodama S, Yachi Y, Heianza Y, Hirasawa R, Ibe Y, et al. Skipping breakfast and prevalence of overweight and obesity in Asian and Pacific regions: a meta-analysis. Prev Med 2011;53(4–5):260–7. https://doi.org/10.1016/j.ypmed.2011.08.030.
- [34] Jang S-H, Suh YS, Chung Y-J. Metabolic risk and nutritional state according to breakfast energy level of Korean adults: using the 2007-2009 Korea National Health and Nutrition Examination Survey. J Nutr Health 2015;48:46-57. https://doi.org/10.4163/jnh.2015.48.1.46.
- [35] Perry RJ, Samuel VT, Petersen KF, Shulman GI. The role of hepatic lipids in hepatic insulin resistance and type 2 diabetes. Nature 2014;510(7503):84–91. https://doi.org/10.1038/nature13478.
- [36] Lackey DE, Olefsky JM. Regulation of metabolism by the innate immune

- system. Nat Rev Endocrinol 2016;12(1):15–28. https://doi.org/10.1038/nrendo.2015.189.
- [37] Ozcan U, Cao Q, Yilmaz E, Lee AH, Iwakoshi NN, Ozdelen E, et al. Endoplasmic reticulum stress links obesity, insulin action, and type 2 diabetes. Science 2004;306(5695):457–61. https://doi.org/10.1126/science.1103160.
- [38] Kahn SE, Hull RL, Utschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 2006;444(7121):840–6. https://doi.org/10.1038/nature05482.
- [39] Lee HJ, Kim CO, Lee DC. Association between daily sunlight exposure and fractures in older Korean adults with osteoporosis: a nationwide populationbased cross-sectional study. Yonsei Med J 2021;62(7):593–9. https://doi.org/ 10.3349/ymj.2021.62.7.593.
- [40] Kalisch T, Wilimzig C, Kleibel N, Tegenthoff M, Dinse HR. Age-related attenuation of dominant hand superiority. PLoS One 2006;1(1):e90. https://doi.org/ 10.1371/journal.pone.0000090.