

Normal Glucose Tolerance with a High 1-Hour Postload Plasma Glucose Level Exhibits Decreased β -Cell Function Similar to Impaired Glucose Tolerance

Tae Jung Oh, Se Hee Min, Chang Ho Ahn, Eun Ky Kim, Soo Heon Kwak, Hye Seung Jung, Kyong Soo Park, Young Min Cho

Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

Background: Subjects with normal glucose tolerance (NGT) who have a high 1-hour postload plasma glucose level (≥ 155 mg/dL; NGT 1 hour-high) have been shown to be at higher risk for type 2 diabetes than subjects with NGT 1 hour-low postload plasma glucose level (< 155 mg/dL). We compared β -cell function in subjects with NGT 1 hour-high, NGT 1 hour-low, and impaired glucose tolerance (IGT).

Methods: We classified subjects into NGT 1 hour-low ($n=149$), NGT 1 hour-high ($n=43$), and IGT ($n=52$). The β -cell function was assessed based on insulinogenic index (IGI), oral disposition index (DI), and insulin secretion-sensitivity index-2 (ISSI-2).

Results: Insulin sensitivity was comparable between the subjects with NGT 1 hour-high and NGT 1 hour-low. The β -cell function with/without adjusting insulin sensitivity was significantly different among the three groups. The IGI (pmol/mmol) was 116.8 ± 107.3 vs. 64.8 ± 47.8 vs. 65.8 ± 80.6 ($P=0.141$), oral DI was 3.5 ± 4.2 vs. 1.8 ± 1.4 vs. 1.8 ± 3.1 ($P<0.001$), and ISSI-2 was 301.2 ± 113.7 vs. 213.2 ± 67.3 vs. 172.5 ± 87.5 ($P<0.001$) in NGT 1 hour-low, NGT 1 hour-high, and IGT, respectively. *Post hoc* analyses revealed that oral DI and ISSI-2 were significantly different between NGT 1 hour-low and NGT 1 hour-high but comparable between NGT 1 hour-high and IGT.

Conclusion: Among Korean subjects with NGT, those who have a higher 1-hour postload glucose level have a compromised insulin-sensitivity adjusted β -cell function to a similar degree as IGT subjects.

Keywords: β -Cell function; Impaired glucose tolerance; Normal glucose tolerance; Oral glucose tolerance test

INTRODUCTION

The prevalence of diabetes is increasing with a changing lifestyle including increased calorie intake and decreased physical activity. Therefore, we have experienced a significant increase in the prevalence of diabetes over the past 40 years in Korea. The prevalence of diabetes was estimated to be 1.5% in the early 1970s, but is currently estimated to be as high as 10% in the adult Korean population [1]. In a 2-year follow-up study conducted in Yonchon county, which included 1,193 subjects without diabetes at baseline, the fasting plasma proinsulin lev-

el was a predictor of incident type 2 diabetes whereas the fasting plasma insulin levels was not [2]. This indicates that β -cell dysfunction rather than insulin resistance is a marker for increased risk of developing type 2 diabetes in non-diabetic Korean adults. In addition, a community cohort study conducted in the Mokdong area in Seoul reported that nondiabetic offspring of diabetic patients showed decreased acute insulin response but comparable insulin sensitivity relative to the matched nondiabetic controls without family history of diabetes [3]. Therefore, nondiabetic subjects with decreased β -cell capacity may have an increased risk of developing type 2 diabetes in

Corresponding author: Young Min Cho
Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, Korea
E-mail: ymchomd@snu.ac.kr
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Korea, which has been reproducibly reported in recent studies performed in Korea [4,5]. In line with this notion, genetic susceptibility to type 2 diabetes is largely related to the polymorphisms in the genes accountable for pancreatic β -cell function in Asians including Koreans [6,7].

In general, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are regarded as indicating prediabetes [8], implying that these conditions are closely related to diabetes in a dysglycemia continuum. However, some subjects with normal glucose tolerance (NGT) may have an increased risk of type 2 diabetes. In the Baltimore Longitudinal Study of Aging [9], most NGT subjects who developed type 2 diabetes turned to IFG and/or IGT during the follow-up. However, a small proportion of NGT subjects (2.5%) progressed directly to diabetes without documented abnormalities in the oral glucose tolerance test (OGTT), which was performed biennially for up to 20 years [9]. Moreover, in a study with 74,309 person-years of follow-up, which was performed by the Israel Defense Forces, NGT subjects with relatively high fasting plasma glucose (FPG) levels (i.e., 87 to 99 mg/dL) were at a progressively increased risk for developing diabetes compared with NGT subjects with relatively low FPG levels (i.e., <81 mg/dL) [10]. Taken together, it is necessary to develop an effective way to identify individuals with an increased risk of future diabetes although they belong to the NGT category.

It has been known that subjects with NGT are heterogeneous with regard to β -cell function and insulin sensitivity [11]. Recently, a subgroup of NGT was suggested by measuring 1-hour postload plasma glucose levels during 75 g OGTTs [12-14]. During the 7 to 8 years of follow-up, 8% to 15% of subjects with NGT who had a 1-hour postload plasma glucose level ≥ 155 mg/dL (NGT 1 hour-high) at baseline developed type 2 diabetes, whereas only 1% to 3% of subjects with NGT who had a 1-hour postload plasma glucose level <155 mg/dL (NGT 1 hour-low) developed type 2 diabetes [13,14]. The cutoff 1-hour postload plasma glucose level of 155 mg/dL exhibited 75% sensitivity and 79% specificity for predicting type 2 diabetes [12]. Furthermore, 1 hour plasma glucose levels had a stronger correlation with insulin secretion and sensitivity indices than FPG or 2 hours plasma glucose levels [12,13]. Therefore, 1-hour plasma glucose levels could be an appropriate parameter for categorizing subjects with NGT who are at risk of developing type 2 diabetes. Although, compared with Caucasian or African counterparts, East Asians have distinct characteristics in glucose metabolism with higher insulin sensitivity and lower insulin secretory ca-

capacity across all glucose tolerance categories encompassing NGT, IFG/IGT, and type 2 diabetes [15], the clinical significance of the NGT 1 hour-high status has not yet been explored. Therefore, we compared metabolic characteristics of NGT 1 hour-high, NGT 1 hour-low, and IGT in Korean populations.

METHODS

The study protocol was approved by the Institutional Review Board at Seoul National University Hospital (registration number: H-1402-006-557). We recruited subjects aged 30 to 80 years by local advertisement. Subjects taking medications for diabetes, hypertension, hyperlipidemia, or obesity as well as pregnant women were excluded. Of the 280 subjects who were screened by means of the standard 75 g OGTT, 192 subjects with NGT, and 52 subjects with IGT were finally included in this study. For the OGTTs, subjects were asked to fast overnight. First, height, body weight, waist and hip circumferences, and systolic and diastolic blood pressures were measured. Then, fasting blood samples were drawn for the measurement of plasma concentrations of glucose, hemoglobin A1c, insulin, C-peptide, total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C). After a 75 g oral glucose load, blood samples were drawn at 30, 60, 90, and 120 minutes to measure plasma levels of glucose and insulin. Informed consent was obtained from all participants prior to any research procedures.

According to 1-hour postload plasma glucose levels, the subjects with NGT were divided into the following two groups: 149 subjects with NGT 1 hour-low (<155 mg/dL) and 43 subjects with NGT 1 hour-high (≥ 155 mg/dL). The homeostasis model assessment of insulin resistance (HOMA-IR) and pancreatic β -cell function (HOMA- β) were calculated by plasma insulin ($\mu\text{U/mL}$) \times plasma glucose (mmol/L)/22.5, and plasma insulin ($\mu\text{U/mL}$) $\times 20 / (\text{plasma glucose [mmol/L]} - 3.5)$, respectively [16]. The insulinogenic index (IGI; pmol/mmol) at 30 or 60 minutes was calculated by (insulin at 30 minutes - insulin at 0 minute) / (glucose at 30 minutes - glucose at 0 minute) and (insulin at 60 minutes - insulin at 0 minute) / (glucose at 60 minutes - glucose at 0 minute), respectively [17]. The oral disposition index (DI) was calculated by $\text{IGI} \times 1 / \text{fasting insulin}$ [18]. The Matsuda index was calculated by $10,000 / \sqrt{(\text{fasting glucose} \times \text{fasting insulin} \times \text{mean glucose} \times \text{mean insulin})}$ [19]. The area under the curve (AUC) was calculated by the trapezoidal rule. The insulin secretion-sensitivity index-2 (ISSI-2) was defined as $\text{AUC}_{\text{insulin}} /$

$AUC_{\text{glucose}} \times \text{Matsuda index}$ [20].

Statistical analyses

The data analysis was performed using SPSS version 21.0 (IBM Co., Armonk, NY, USA). Values are presented as mean \pm standard deviation. The chi-square test was adopted to compare the sex distribution. Parameters that were not normally distributed were log transformed before analysis. One-way analysis of variance followed by Games-Howell *post hoc* test was used to compare the clinical and biochemical parameters. Next, an analysis of covariance (ANCOVA) test was used to adjust the effect of sex and body mass index (BMI). Sex-adjusted partial correlation tests were used to evaluate the correlations between parameters. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows the clinical and biochemical characteristics of

the study subjects. Age was comparable between the three groups, but more female subjects were included in the NGT 1 hour-low group. In addition, BMI was also different among the three groups. Accordingly, we analyzed the data with adjustment of sex and BMI. FPG levels were 85.6 ± 6.0 , 89.1 ± 6.8 , 93.7 ± 12.5 mg/dL in the NGT 1 hour-low group, the NGT 1 hour-high group, and the IGT group, respectively ($P < 0.001$, with or without sex and BMI adjustment). One-hour postload plasma glucose levels were 115.3 ± 23.7 , 182.6 ± 22.8 , 195.2 ± 34.8 mg/dL in the NGT 1 hour-low group, the NGT 1 hour-high group, and the IGT group, respectively ($P < 0.001$, with or without sex and BMI adjustment) and *post hoc* analysis revealed that 1-hour plasma glucose was significantly different between the NGT 1 hour-low and the NGT 1 hour-high groups. Fasting C-peptide levels were gradually increased from the NGT 1 hour-low group to the IGT group (1.5 ± 0.5 , 1.6 ± 0.8 , and 1.9 ± 0.9 ng/mL, $P = 0.031$ and $P = 0.126$ without and with sex and BMI adjustment, respectively). Triglyceride levels were significantly different among groups, but they were comparable after

Table 1. Clinical and biochemical characteristics of study subjects

Characteristic	NGT 1 hour-low (<i>n</i> = 149)	NGT 1 hour-high (<i>n</i> = 43)	IGT (<i>n</i> = 52)	<i>P</i> value	Adjusted <i>P</i> value ^a
Age, yr	52.8 \pm 7.0	53.7 \pm 7.0	54.3 \pm 7.4	0.389	0.599
Sex, male:female	32:117	14:29	30:22	<0.001	NA
Body mass index, kg/m ²	23.8 \pm 2.8 ^b	24.5 \pm 3.2 ^{bc}	25.2 \pm 3.2 ^c	0.009	NA
Waist-to-hip ratio	0.85 \pm 0.07 ^b	0.87 \pm 0.05 ^{bc}	0.87 \pm 0.05 ^c	0.009	0.476
Systolic blood pressure, mm Hg	107.9 \pm 17.1	112.3 \pm 16.5	114.1 \pm 17.2	0.160	0.996
Diastolic blood pressure, mm Hg	69.6 \pm 12.7	71.8 \pm 11.7	72.6 \pm 14.4	0.746	0.905
Fasting plasma glucose, mg/dL	85.6 \pm 6.0 ^b	89.1 \pm 6.8 ^c	93.7 \pm 12.5 ^c	<0.001	<0.001
1-Hour plasma glucose, mg/dL	115.3 \pm 23.7 ^b	182.6 \pm 22.8 ^c	195.2 \pm 34.8 ^c	<0.001	<0.001
2-Hour plasma glucose, mg/dL	101.0 \pm 18.0 ^b	116.1 \pm 16.8 ^c	163.4 \pm 18.8 ^c	<0.001	<0.001
HbA1c, %	5.3 \pm 0.3 ^b	5.4 \pm 0.3 ^b	5.6 \pm 0.7 ^c	<0.001	<0.001
Fasting plasma insulin, μ U/mL	5.8 \pm 2.8	6.2 \pm 4.4	7.1 \pm 4.7	0.293	0.332
Fasting plasma C-peptide, ng/mL	1.5 \pm 0.5 ^b	1.6 \pm 0.8 ^{bc}	1.9 \pm 0.9 ^c	0.031	0.126
Total cholesterol, mg/dL	187.1 \pm 28.5	198.8 \pm 29.6	195.4 \pm 35.7	0.060	0.082
Triglyceride, mg/dL	109.4 \pm 74.4 ^b	120.3 \pm 74.7 ^c	151.7 \pm 105.9 ^c	0.017	0.476
LDL-C, mg/dL	116.3 \pm 27.3	121.3 \pm 29.9	122.0 \pm 36.8	0.673	0.760
HDL-C, mg/dL	46.7 \pm 11.0	46.5 \pm 11.9	43.8 \pm 9.2	0.317	0.101

Values are presented as mean \pm standard deviation. *P* values were calculated after normalizing log transformation using one-way analysis of variance except for sex, which was calculated by the chi-square test.

NGT, normal glucose tolerance; IGT, impaired glucose tolerance; NA, not applicable; HbA1c, hemoglobin A1c; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

^aSex and body mass index (BMI) adjusted *P* values were calculated after normalizing log transformation using analysis of covariance with age and BMI as covariates, ^{bc}The data with different superscript letters are significantly different ($P < 0.05$) according to the Games-Howell *post hoc* test.

sex and BMI adjustment.

Parameters of β -cell function, insulin resistance (or insulin sensitivity), and β -cell function adjusted by insulin resistance are

presented in Table 2. Insulin secretory function assessed by IGI at 30 or 60 minutes was not significantly different among groups. Both HOMA- β -cell and HOMA-IR values were comparable

Table 2. Parameters of β -cell function, insulin resistance (or insulin sensitivity) and β -cell function adjusted by insulin resistance

	NGT 1 hour-low (n=149)	NGT 1 hour-high (n=43)	IGT (n=52)	P value	Adjusted P value ^a
Insulinogenic index (pmol/mmol) at 30 min	116.8±107.3	64.8±47.8	65.8±80.6	0.141	0.101
Insulinogenic index (pmol/mmol) at 60 min	137.6±815.9	79.8±54.8	71.8±82.2	0.815	0.917
HOMA- β -cell	102.7±52.9	92.5±61.7	96.3±66.3	0.148	0.197
HOMA-IR	1.2±0.6	1.4±1.0	1.7±1.2	0.076	0.133
Matsuda index	9.3±4.9 ^b	8.3±6.1 ^{b,c}	6.5±4.7 ^c	<0.001	<0.001
Oral disposition index	3.5±4.2 ^b	1.8±1.4 ^c	1.8±3.1 ^c	<0.001	<0.001
ISSI-2	301.2±113.7 ^b	213.2±67.3 ^c	172.5±87.5 ^d	<0.001	<0.001

Values are presented as mean±standard deviation. P values were calculated after normalizing log transformation using one-way analysis of variance.

NGT, normal glucose tolerance; IGT, impaired glucose tolerance; HOMA- β , homeostasis model assessment of pancreatic β -cell; HOMA-IR, homeostasis model assessment of insulin resistance; ISSI-2, insulin secretion-sensitivity index-2.

^aSex and body mass index (BMI) adjusted P values were calculated after normalizing log transformation using analysis of covariance with age and BMI as covariates, ^{b,c,d}The data with different superscript letters are significantly different (P<0.05) according to the Games-Howell *post hoc* test.

Table 3. Sex-adjusted partial correlation between plasma glucose levels and biochemical parameters or cardiovascular risk profiles

Variable	Fasting plasma glucose		1-Hour plasma glucose level		2-Hour plasma glucose level	
	r	P value	r	P value	r	P value
Insulinogenic index at 30 min	-0.100	0.121	-0.380	<0.001	-0.226	<0.001
Insulinogenic index at 60 min	-0.074	0.259	-0.071	0.279	-0.138	0.033
HOMA- β -cell	-0.358	<0.001	-0.112	0.082	0.023	0.745
HOMA-IR	0.380	<0.001	0.206	0.001	0.255	<0.001
Matsuda index	-0.338	<0.001	-0.274	<0.001	-0.234	<0.001
Oral disposition index	-0.091	0.157	-0.351	<0.001	-0.233	<0.001
ISSI-2	-0.385	<0.001	-0.565	<0.001	-0.517	<0.001
BMI	0.184	0.004	0.210	0.001	0.242	<0.001
Waist circumference	0.189	0.004	0.231	<0.001	0.260	<0.001
WHR	0.070	0.276	0.155	0.016	0.195	0.002
Systolic blood pressure	0.166	0.010	0.104	0.107	0.027	0.673
Diastolic blood pressure	0.150	0.020	0.095	0.141	0.024	0.711
Total cholesterol	0.043	0.503	0.237	<0.001	0.154	0.016
Triglyceride	0.162	0.012	0.173	0.007	0.204	0.001
LDL-C	0.079	0.220	0.186	0.004	0.134	0.037
HDL-C	-0.161	0.012	-0.078	0.229	-0.064	0.321

P values were calculated using sex-adjusted partial correlation and r is partial correlation coefficient.

HOMA- β , homeostasis model assessment of pancreatic β -cell; HOMA-IR, homeostasis model assessment of insulin resistance; ISSI-2, insulin secretion-sensitivity index-2; BMI, body mass index; WHR, waist-to-hip ratio; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol.

among the three groups (Table 2). The Matsuda index was significantly different among groups, but the post hoc analysis revealed that the difference was comparable between the NGT 1 hour-low group and the NGT 1 hour-high group (Table 2). The oral DI and the ISSI-2, which represent β -cell function with adjustment for insulin resistance, were significantly different among the three groups. The post hoc test showed that oral DI and ISSI-2 were significantly different between the NGT 1 hour-low group and the NGT 1 hour-high group (Table 2).

Table 3 shows the sex-adjusted partial correlation coefficients between clinical/metabolic parameters and either the FPG levels, 1-hour postload plasma glucose levels, and 2-hour postload plasma glucose levels. In general, the patterns of correlation appeared to be similar among three glycemic parameters such as fasting, 1-hour postload, and 2-hour postload plasma glucose levels. The 1-hour postload glucose level exhibited a significant correlation with all of the clinical/metabolic parameters except IGI at 60 minutes, HOMA- β -cell, blood pressure, and HDL-C.

DISCUSSION

In this study, β -cell function, insulin resistance (or insulin sensitivity) and indices of insulin secretion adjusted by the degree of insulin resistance were similar between the NGT 1 hour-high group and the IGT group. However, between the NGT 1 hour-low and the NGT 1 hour-high groups, there was a distinct difference in β -cell function adjusted by insulin sensitivity such as oral DI and ISSI-2 with comparable insulin sensitivity. In other words, subjects with NGT can be divided into two discrete groups based on β -cell function even in the Korean population.

In Caucasians, the NGT 1 hour-high group exhibited both decreased β -cell function and reduced insulin sensitivity compared to the NGT 1 hour-low group [21]. In contrast, the NGT 1 hour-high group in this study showed impaired β -cell function with relatively preserved insulin sensitivity relative to the NGT 1 hour-low group. Because the sample size of our current study was relatively small, we may not have been able to detect a difference in insulin sensitivity between the NGT 1-hour high/low groups. However, there is evidence for the dissociation in β -cell function and insulin sensitivity in Korean subjects with a high risk for type 2 diabetes. For example, impaired β -cell function assessed by fasting plasma proinsulin levels [2], acute insulin response during the frequently sampled intravenous glucose tolerance test [3], and IGI measured

during the OGTT [22] was significantly associated with the clinical characteristics of subjects who developed type 2 diabetes in 2 years, subjects who were offspring of diabetic patients, and subjects with earlier stages of glucose intolerance, respectively. However, indices for insulin sensitivity did not show any statistical association with regard to the conditions listed above [2,3,22]. Taken together, the NGT 1-hour high group may represent a unique group of subjects with impaired β -cell function that have an increased risk of future type 2 diabetes in Koreans.

Elevated 1-hour plasma glucose levels have been reported to be related with an increase in cardiovascular risk [23,24]. The NGT 1-hour high group had a higher systolic blood pressure [23], higher LDL-C and triglyceride levels, lower HDL-C levels [24], and higher pulse wave velocity [23] than the NGT 1 hour-low group. In addition, 1-hour plasma glucose levels were significantly correlated with brachial-ankle pulse wave velocity [25] and carotid intima-media thickness [26]. We also observed that 1-hour plasma glucose levels exhibited significant correlation with BMI, waist circumference, WHR, and total and LDL-C levels. Therefore, 1-hour plasma glucose levels could be a useful marker for cardiovascular disease in Koreans, which needs to be explored in future studies.

To our knowledge, this is the first study examining the relationship between 1-hour plasma glucose levels with insulin secretory function in East Asian populations. However, because of the cross-sectional nature of this study, we cannot conclude whether the NGT 1 hour-high group has a higher risk for developing diabetes. The relatively small sample size, possible selection bias by recruiting subjects using local advertisement, and unequal sex distribution may limit the generalization of our results. In addition, we were unable to see the effect of different genetic makeup on insulin secretory function and insulin sensitivity. Importantly, this study was not designed to identify a cutoff of the 1-hour plasma glucose level, which predicts future development of prediabetes or diabetes in Koreans. However, there is a growing body of evidence supporting that the cutoff value for 1-hour plasma glucose level of 155 mg/dL might be universally implicated in predicting the risk for diabetes regardless of ethnic background. From the data of Asian Indians, diabetes and prediabetes were more prevalent in subjects with higher 1-hour plasma glucose levels during the 13 years of follow-up [27]. In other population with obese Latino youth with a family history of type 2 diabetes [28] and Finnish businessman [29], 1-hour plasma glucose

levels also showed high prediction power of β -cell deterioration and development of diabetes over 8 years of follow-up and 34 years of follow-up, respectively. Although we do not know if the cutoff of 155 mg/dL is optimal for Koreans, this cutoff successfully differentiated two metabolically different groups in this study. Nevertheless, future longitudinal studies are necessary to investigate the predictive power of the 1-hour postload plasma glucose level for the development of type 2 diabetes in Koreans.

In conclusion, subjects with NGT can be further categorized by postload 1-hour plasma glucose levels with a cutoff of 155 mg/dL. The NGT 1-hour high group may represent a distinct group with impaired β -cell function adjusted by insulin sensitivity at a degree similar to the IGT group. Measurement of postload 1-hour plasma glucose levels during an OGTT would be useful in counseling patients at risk for developing type 2 diabetes. Now, it is the time to revisit the OGTT data from longitudinal cohorts in Korea with specific regard to the postload 1-hour plasma glucose level. Furthermore, prospective studies are necessary to examine the role of the postload 1-hour plasma glucose level in predicting the risk for developing type 2 diabetes and cardiovascular disease in Koreans.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

- Kim DJ. The epidemiology of diabetes in Korea. *Diabetes Metab J* 2011;35:303-8.
- Shin CS, Lee HK, Koh CS, Kim YI, Shin YS, Yoo KY, Paik HY, Park YS, Yang BG. Risk factors for the development of NIDDM in Yonchon County, Korea. *Diabetes Care* 1997;20:1842-6.
- Song J, Oh JY, Sung YA, Pak YK, Park KS, Lee HK. Peripheral blood mitochondrial DNA content is related to insulin sensitivity in offspring of type 2 diabetic patients. *Diabetes Care* 2001;24:865-9.
- Rhee SY, Kwon MK, Park BJ, Chon S, Jeong IK, Oh S, Ahn KJ, Chung HY, Kim SW, Kim JW, Kim YS, Woo JT. Differences in insulin sensitivity and secretory capacity based on OGTT in subjects with impaired glucose regulation. *Korean J Intern Med* 2007;22:270-4.
- Choi ES, Rhee EJ, Kim JH, Won JC, Park CY, Lee WY, Oh KW, Park SW, Kim SW. Insulin sensitivity and insulin secretion determined by homeostasis model assessment and future risk of diabetes mellitus in Korean men. *Korean Diabetes J* 2008;32:498-505.
- Ng MC, Park KS, Oh B, Tam CH, Cho YM, Shin HD, Lam VK, Ma RC, So WY, Cho YS, Kim HL, Lee HK, Chan JC, Cho NH. Implication of genetic variants near TCF7L2, SLC30A8, HHEX, CDKAL1, CDKN2A/B, IGF2BP2, and FTO in type 2 diabetes and obesity in 6,719 Asians. *Diabetes* 2008;57:2226-33.
- Cho YS, Chen CH, Hu C, Long J, Ong RT, Sim X, Takeuchi F, Wu Y, Go MJ, Yamauchi T, Chang YC, Kwak SH, Ma RC, Yamamoto K, Adair LS, Aung T, Cai Q, Chang LC, Chen YT, Gao Y, Hu FB, Kim HL, Kim S, Kim YJ, Lee JJ, Lee NR, Li Y, Liu JJ, Lu W, Nakamura J, Nakashima E, Ng DP, Tay WT, Tsai FJ, Wong TY, Yokota M, Zheng W, Zhang R, Wang C, So WY, Ohnaka K, Ikegami H, Hara K, Cho YM, Cho NH, Chang TJ, Bao Y, Hedman AK, Morris AP, McCarthy MI; DIAGRAM Consortium; MuTHER Consortium, Takayanagi R, Park KS, Jia W, Chuang LM, Chan JC, Maeda S, Kadowaki T, Lee JY, Wu JY, Teo YY, Tai ES, Shu XO, Mohlke KL, Kato N, Han BG, Seielstad M. Meta-analysis of genome-wide association studies identifies eight new loci for type 2 diabetes in east Asians. *Nat Genet* 2012;44:67-72.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;37 Suppl 1:S81-90.
- Meigs JB, Muller DC, Nathan DM, Blake DR, Andres R; Baltimore Longitudinal Study of Aging. The natural history of progression from normal glucose tolerance to type 2 diabetes in the Baltimore Longitudinal Study of Aging. *Diabetes* 2003;52:1475-84.
- Tirosh A, Shai I, Tekes-Manova D, Israeli E, Pereg D, Shochat T, Kochba I, Rudich A; Israeli Diabetes Research Group. Normal fasting plasma glucose levels and type 2 diabetes in young men. *N Engl J Med* 2005;353:1454-62.
- Kahn SE, Prigeon RL, McCulloch DK, Boyko EJ, Bergman RN, Schwartz MW, Neifing JL, Ward WK, Beard JC, Palmer JP, et al. Quantification of the relationship between insulin sensitivity and beta-cell function in human subjects. Evidence for a hyperbolic function. *Diabetes* 1993;42:1663-72.
- Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? *Diabetes Care* 2007;30:1544-8.
- Abdul-Ghani MA, Lyssenko V, Tuomi T, DeFronzo RA, Groop L. Fasting versus postload plasma glucose concentration and the risk for future type 2 diabetes: results from the Botnia

- Study. *Diabetes Care* 2009;32:281-6.
14. Abdul-Ghani MA, Abdul-Ghani T, Ali N, DeFronzo RA. One-hour plasma glucose concentration and the metabolic syndrome identify subjects at high risk for future type 2 diabetes. *Diabetes Care* 2008;31:1650-5.
 15. Kodama K, Tojjar D, Yamada S, Toda K, Patel CJ, Butte AJ. Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis. *Diabetes Care* 2013;36:1789-96.
 16. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412-9.
 17. Seltzer HS, Allen EW, Herron AL Jr, Brennan MT. Insulin secretion in response to glycemic stimulus: relation of delayed initial release to carbohydrate intolerance in mild diabetes mellitus. *J Clin Invest* 1967;46:323-35.
 18. Utzschneider KM, Prigeon RL, Faulenbach MV, Tong J, Carr DB, Boyko EJ, Leonetti DL, McNeely MJ, Fujimoto WY, Kahn SE. Oral disposition index predicts the development of future diabetes above and beyond fasting and 2-h glucose levels. *Diabetes Care* 2009;32:335-41.
 19. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. *Diabetes Care* 1999;22:1462-70.
 20. Retnakaran R, Qi Y, Goran MI, Hamilton JK. Evaluation of proposed oral disposition index measures in relation to the actual disposition index. *Diabet Med* 2009;26:1198-203.
 21. Marini MA, Succurro E, Frontoni S, Mastroianni S, Arturi F, Sciacqua A, Lauro R, Hribal ML, Perticone F, Sesti G. Insulin sensitivity, beta-cell function, and incretin effect in individuals with elevated 1-hour postload plasma glucose levels. *Diabetes Care* 2012;35:868-72.
 22. Kim DJ, Lee MS, Kim KW, Lee MK. Insulin secretory dysfunction and insulin resistance in the pathogenesis of Korean type 2 diabetes mellitus. *Metabolism* 2001;50:590-3.
 23. Sciacqua A, Maio R, Miceli S, Pascale A, Carullo G, Grillo N, Arturi F, Sesti G, Perticone F. Association between one-hour post-load plasma glucose levels and vascular stiffness in essential hypertension. *PLoS One* 2012;7:e44470.
 24. Bianchi C, Miccoli R, Trombetta M, Giorgino F, Frontoni S, Faioia E, Marchesini G, Dolci MA, Cavalot F, Cavallo G, Leonetti F, Bonadonna RC, Del Prato S; GENFIEV Investigators. Elevated 1-hour postload plasma glucose levels identify subjects with normal glucose tolerance but impaired beta-cell function, insulin resistance, and worse cardiovascular risk profile: the GENFIEV study. *J Clin Endocrinol Metab* 2013;98:2100-5.
 25. Nijijima K, Muranaka Y, Ando T, Okada S, Nijijima Y, Hashimoto K, Yamada M, Ohshima K, Mori M, Ono K. Elevated 1-h plasma glucose following 75-g oral glucose load is a predictor of arterial stiffness in subjects with normal glucose tolerance. *Diabet Med* 2012;29:e457-60.
 26. Succurro E, Marini MA, Arturi F, Grembiale A, Lugara M, Andreozzi F, Sciacqua A, Lauro R, Hribal ML, Perticone F, Sesti G. Elevated one-hour post-load plasma glucose levels identifies subjects with normal glucose tolerance but early carotid atherosclerosis. *Atherosclerosis* 2009;207:245-9.
 27. Priya M, Anjana RM, Chivanga FS, Gokulakrishnan K, Deepa M, Mohan V. 1-hour venous plasma glucose and incident pre-diabetes and diabetes in Asian Indians. *Diabetes Technol Ther* 2013;15:497-502.
 28. Kim YG, Hahn S, Oh TJ, Kwak SH, Park KS, Cho YM. Differences in the glucose-lowering efficacy of dipeptidyl peptidase-4 inhibitors between Asians and non-Asians: a systematic review and meta-analysis. *Diabetologia* 2013;56:696-708.
 29. Strandberg AY, Pienimaki T, Pitkala KH, Tilvis RS, Salomaa VV, Strandberg TE. Comparison of normal fasting and one-hour glucose levels as predictors of future diabetes during a 34-year follow-up. *Ann Med* 2013;45:336-40.