Clinical characteristics of insulin resistance and insulin secretory capacity in Korean person with type 2 diabetes

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ABSTRACT

- Background:** Type 2 diabetes is a common multigenic disorder which caused by impaired β-cell function and insulin sensitivity. However, which of the two is the primary defect is much debated. In addition, the rapid increase in diabetes in Asia in a short period may be due to the increase in obesity.
- Aim:** We evaluated the clinical characteristic of insulin resistance and the insulin secretion capacity in newly diagnosed, drug-naive Korean persons with type 2 diabetes by analyzing a nationwide cross-sectional primary care clinic-based study.
- Method:** We conducted a study of 912 drug-naive patients (512 men and 400 women) with newly diagnosed diabetes from primary care clinics nationwide in 2015-2016. All participants underwent a 75g OGTT after an overnight fast of 10–12h. We assessed insulin resistance using the homeostasis model assessment of insulin resistance (HOMA-IR) and insulin secretion based on fasting serum C-peptide level. The presence of insulin resistance was defined as a HOMA-IR ≥2.5 and insulin secretory dysfunction was classified based on fasting plasma C-peptide levels: severe (<1.10 ng/ml), moderate (1.10–1.69 ng/ml), and mild to non-secretory defect (≥1.70 ng/ml).
- Results:** A total of 75.1 and 22.6% of participants had insulin resistance and β-cell dysfunction, respectively. The proportion of participants with insulin resistance but no β-cell dysfunction increased and the proportion of participants with β-cell dysfunction but no insulin resistance decreased as body mass index (BMI) increased. People diagnosed with diabetes before 40 years of age had significantly higher HOMA-IR and BMI than those diagnosed over 65 years of age (HOMA-IR, 5.0 vs. 3.0; BMI, 28.7 vs. 25.1 kg/m²).
- Discussion:** We observed that the main pathogenic mechanism of type 2 diabetes is insulin resistance in participants with newly diagnosed type 2 diabetes. In addition, young adults with diabetes are more likely to have higher insulin resistance with obesity and have higher insulin secretory defect with severe hyperglycemia in the early period of diabetes than older populations.

INTRODUCTION

- Type 2 diabetes in East Asia**, including South Korea, is **characterized primarily by β-cell dysfunction**.
- However, **the prevalence of diabetes has increased in conjunction with the incidence of obesity** in South Korea and previous studies have reported that **insulin resistance is the dominant factor** in the development of type 2 diabetes due to lifestyle changes.
- We evaluated **the clinical characteristics of insulin resistance and the insulin secretion capacity of newly diagnosed, drug-naive people with type 2 diabetes in 2015–2016** by analyzing nationwide cross-sectional data.

METHODS

- Study population**
 - A cross-sectional study that included **83 primary care clinics and hospitals** from different areas in South Korea was conducted.
 - All individuals who visited each clinic or hospital from August 2015 to May 2016 and whose type 2 diabetes had been diagnosed within one year.
 - The present analysis **912 participants (512 men and 400 women)** who underwent health examinations.
- Indicators of glucose metabolism**
 - Insulin sensitivity index
 - HOMA-IR: $G_0 \text{ (mg/dL)} \times I_0 \text{ (uIU/mL)} / 405$
 - Insulin secretion index
 - HOMA-β: $360 \times I_0 / (G_0 - 63)$
 - Insulinogenic index (IGI): $\Delta I_{30} / \Delta G_{30}$
 - Disposition index: insulinogenic index $\times 1 / I_0$
 - Fasting C-peptide (ng/mL)
 - The presence of insulin resistance was defined as a HOMA-IR value ≥ 2.5 .
 - The presence of insulin secretory defect was defined as fasting C-peptide levels $< 1.70 \text{ ng/mL}$.
- Definition of obesity**
 - Underweight: BMI $< 18.5 \text{ kg/m}^2$
 - Normal weight: BMI $18.5\text{--}22.9 \text{ kg/m}^2$
 - Overweight: BMI $23.0\text{--}24.9 \text{ kg/m}^2$
 - Obese class I: BMI $25.0\text{--}29.9 \text{ kg/m}^2$
 - Obese class II: BMI $\geq 30.0 \text{ kg/m}^2$

RESULTS

Table 1. Characteristics of the study participants by age groups

	Age, years			p-value
	<40 (n = 81)	40-64 (n = 604)	≥65 (n = 227)	
Age, years	33.6 ± 4.9	53.8 ± 6.5	71.0 ± 4.9	<0.001
Men, n (%)	60 (74.1)	356 (58.9)	96 (42.3)	<0.001
Body mass index, kg/m²	28.7 ± 4.9	25.8 ± 3.6	25.1 ± 3.2	<0.001
Waist circumference, cm*	94.4 ± 12.6	88.1 ± 9.0	88.4 ± 8.8	<0.001
Systolic blood pressure, mmHg	132.2 ± 15.1	129.2 ± 13.9	130.2 ± 13.9	0.174
Diastolic blood pressure, mmHg	84.4 ± 12.4	80.7 ± 10.0	77.5 ± 8.2	<0.001
Fasting glucose, mg/dL	172.0 [115.0-251.0]	136.0 [113.0-182.0]	121.0 [109.0-137.0]	<0.001
30-min glucose, mg/dL	248.0 [203.0-347.0]	228.0 [196.0-283.5]	207.0 [183.0-235.0]	<0.001
Fasting insulin, uIU/mL	11.3 [8.0-16.7]	10.2 [7.7-13.7]	9.7 [7.5-12.9]	0.037
30-min insulin, uIU/mL	16.9 [10.8-30.5]	19.9 [12.9-31.5]	23.3 [14.7-33.2]	0.047
Fasting C-peptide, ng/mL	2.8 [1.8-3.8]	2.4 [1.8-3.1]	2.2 [1.6-3.0]	0.031
30-min C-peptide, ng/mL	4.1 [2.3-5.4]	3.7 [2.8-5.1]	3.9 [3.0-5.7]	0.236
Measures of beta cell function				
HOMA-β	39.3 [16.3-99.4]	51.7 [28.1-83.2]	64.9 [43.6-93.6]	<0.001
Insulinogenic index	10.3 [2.2-28.0]	13.4 [4.9-27.9]	18.7 [8.6-31.6]	0.003
Disposition index	0.15 [0.03-0.33]	0.19 [0.07-0.37]	0.25 [0.12-0.49]	<0.001
HOMA-IR	5.0 [3.4-6.7]	3.6 [2.6-5.3]	3.0 [2.2-4.2]	<0.001
HbA1C, %	9.2 [6.6-11.2]	7.0 [6.3-8.9]	6.6 [6.1-7.6]	<0.001
HbA1C, n (%)				
<6.5	17 (21.0)	199 (32.9)	107 (47.1)	<0.001
6.5-6.9	9 (11.1)	96 (15.9)	40 (17.6)	
7.0-7.9	9 (11.1)	115 (19.0)	38 (16.7)	
8.0-8.9	4 (4.9)	50 (8.3)	17 (7.5)	
9.0-9.9	8 (9.9)	51 (8.4)	9 (4.0)	
≥10	34 (42.0)	93 (15.4)	16 (7.0)	
Total cholesterol, mg/dL	222.2 ± 74.1	198.1 ± 44.3	190.6 ± 43.0	<0.001
HDL cholesterol, mg/dL	42.8 ± 10.0	49.6 ± 13.8	53.3 ± 14.4	<0.001
LDL cholesterol, mg/dL	147.0 ± 73.3	117.8 ± 42.7	108.2 ± 41.8	<0.001
Triglycerides, mg/dL	155.0 [120.0-300.0]	140.5 [98.5-220.5]	130.0 [98.0-190.0]	0.002
Use of antihypertensive drugs, n (%)	13 (16.0)	223 (36.9)	122 (53.7)	<0.001
Use of lipid-lowering drugs, n (%)	18 (22.2)	167 (27.6)	79 (34.8)	0.049
Metabolic syndrome, n (%)*	60 (75.0)	392 (65.3)	141 (62.7)	0.135
Dietary therapy, n (%)	7 (8.6)	77 (12.7)	42 (18.5)	0.037
Physical activity, n (%)	14 (17.3)	150 (24.8)	70 (30.8)	0.041
Current smoker, n (%)	34 (42.0)	165 (27.3)	25 (11.0)	<0.001
Current drinker, n (%)	52 (64.2)	321 (53.1)	73 (32.2)	<0.001

Data are means ± SD or median [25th–75th percentile] unless otherwise indicated.
HbA1C, glycated hemoglobin; HOMA-β, homeostatic model assessment of β-cell function; HOMA-IR, homeostatic model assessment of insulin resistance
*Only 80 people aged <40 years, 600 people aged 40-64 years, and 225 people aged ≥65 years were measured.

Table 2. The proportion of study participants according to insulin resistance and insulin secretion

	n (%)	C-peptide levels, ng/mL			Total
		<1.10	1.10-1.69	≥1.70	
HOMA-IR	≥2.5	8 (0.9)	62 (6.8)	615 (67.4)	685 (75.1)
	<2.5	32 (3.5)	104 (11.4)	91 (10.0)	227 (24.9)
	Total	40 (4.4)	166 (18.2)	706 (77.4)	912 (100.0)

Figure 1. The proportion of insulin resistance (HOMA-IR ≥2.5) and β-cell dysfunction (C-peptide <1.70 ng/mL) according to body mass index and age groups.

CONCLUSION

This analysis of nationwide cross-sectional data from South Korea suggested that **the main pathogenesis in participants with newly diagnosed type 2 diabetes is insulin resistance**.

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