

Body Mass Index and Waist Circumference According to Glucose Tolerance Status in Korea: The 2005 Korean Health and Nutrition Examination Survey

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The purpose of this study was to investigate the stage of glucose intolerance in which persons showed a maximum obesity in Korea. A total of 4,479 participants, who were involved in the 2005 Korean National Health and Nutrition Examination Survey, was examined. The participants were divided into 5 groups by fasting plasma glucose (FPG); normal fasting glucose (NFG)1, FPG < 90 mg/dL; NFG2, FPG 90-99 mg/dL; impaired fasting glucose (IFG)1, FPG 100-109 mg/dL; IFG2, FPG 110-125 mg/dL; and diabetes mellitus, FPG \geq 126 mg/dL or with anti-diabetes drugs. In those with FPG < 110 mg/dL, body mass index (BMI) and waist circumference (WC) were increased with increase of FPG (BMI in men; NFG1, 23.3 ± 0.1 ; NFG2, 24.4 ± 0.1 ; IFG1, 25.0 ± 0.2 kg/m², in women; NFG1, 23.0 ± 0.1 ; NFG2, 24.0 ± 0.1 ; IFG1, 24.8 ± 0.2 kg/m², WC in men; NFG1, 82.1 ± 0.3 ; NFG2, 85.3 ± 0.3 ; IFG1, 86.7 ± 0.5 cm, in women; NFG1, 77.1 ± 0.2 ; NFG2, 79.4 ± 0.3 ; IFG1, 81.8 ± 0.6 cm). In IFG2 and diabetes range, there was no more increase of BMI and WC with increase of FPG in each sex. The data suggest that degree of obesity increases with an increase of FPG in range of FPG < 100 mg/dL, peaked in FPG of 100-109 mg/dL, and then plateaus in higher FPG range in general Korean population.

Key Words: Body Mass Index; Waist Circumference; Diabetes Mellitus; Korea

INTRODUCTION

Obesity and weight gain are associated with an increased risk of developing diabetes (1-3). Weight control is important in the management of diabetes and prevention of developing diabetes in pre-diabetic individuals (4, 5). Visceral adiposity and waist circumference are, also, strong risk factors for type 2 diabetes (6, 7) and an increased waist circumference was associated with diabetes incidence in impaired fasting glucose (IFG) range (6).

Despite lower body mass index (BMI), some Asian countries have similar or even higher prevalence of diabetes than Western countries (8). Several studies about the association obesity with diabetes prevalence in Korean population showed similar results (9, 10). These data suggested that the risk of type 2 diabetes starts at a lower BMI for Asians than for Europeans (11). In previous study including 370 oral glucose tolerance data, we found that the worsening from normal glucose tolerance (NGT) to impaired glucose tolerance (IGT) was more closely related to impaired early-phase insulin secretion than insulin resistance in Korean population (12). Fukushima et al., also, found that at all stages of glucose intolerance, Japanese individuals had reduced early and late phases of insulin responses (13). In Japanese men with NGT, even a small increase in BMI produced a

decrease in beta cell function disproportionate to that in insulin resistance (14).

Many Western studies showed that before development of diabetes, body weight increases progressively, reaching a maximum at the time of diagnosis, and then it tends to decrease after diagnosis (6, 15-21). Although few studies reported about the association between weight changes and diabetes in Korea (22-24), all of their participants were persons who visited out-patients clinic in university hospitals. With limitations of selection bias, the result could not be generalized in Korean population across the nation.

We hypothesized that the stage of reaching a maximal obesity in the course of deterioration from normal glucose to diabetes could be different between Western and Korean population if Koreans have relatively smaller capacity of insulin secretion to compensate increased insulin resistance according to obesity. The purpose of this study is to investigate the stage of glucose intolerance participants showed a maximum obesity. So, we tried to examine the association of body mass index (BMI) and waist circumference (WC) with glucose tolerance status in a nationwide representative population using the 2005 Korean National Health and Nutrition Examination Survey (KNHANES) data.

MATERIALS AND METHODS

Study population

This study was based on the data obtained from the third Korea National Health and Nutrition Examination Survey (KNHANES 2005) among non-institutionalized civilians in the Republic of Korea, which was conducted by the Korean Ministry of Health and Welfare in 2005. This survey was a nationwide representative study using a stratified, multistage probability sampling design for the selection of household units. The survey consisted of health interview, health behavior, health examination, nutrition components. A total of 34,145 individuals from these sampling frames were included in the health interview survey. Among them, 5,531 persons were identified as participants with laboratory test and nutritional survey data. We included only participants older than 25 yr for excluding the possibilities of type 1 DM. Participants with history of cancer, cerebrovascular disease, end stage renal disease, liver cirrhosis, and thyroid disease were excluded because of its effect on weight. Finally, 4,479 persons aged 26-99 yr were identified as participants.

The participants were divided into five groups by fasting plasma glucose (FPG); normal fasting glucose (NFG)1, FPG < 90 mg/dL; NFG2, FPG 90-99; impaired fasting glucose (IFG)1, FPG 100-109; IFG2, FPG 110-125; DM: FPG ≥ 126 or those with anti-diabetes drugs. Clinical practice guidelines for type 2 diabetes in Korea 2011 recommended screening methods differently according to stage of IFG (stage 1, FPG 100-109 mg/dL, stage2: FPG 110-125) (25). So we divided our IFG participants into two groups according to above mentioned criteria. In case of NFG, we grouped our NFG participants by 10 mg/dL from FPG of 100 mg/dL arbitrarily.

Health examination survey and laboratory test

Trained interviewers visited each participant's dwelling and administered a standardized questionnaire on smoking and alcohol consumption. Height and weight were obtained using standardized techniques and equipment. Height was measured to the nearest 0.1 cm using a portable stadiometer (Seriter, Bismarck, ND). Weight was measured to the nearest 0.1 kg using a calibrated balance-beam scale (Giant-150N; Hana, Seoul, Korea). BMI was calculated by dividing weight by height squared (kg/m²). WC was measured on standing participants with a soft tape midway between the lowest rib and the iliac crest. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by standard methods using a sphygmomanometer with the patient in a sitting position. Three measurements were made on all subjects at 5-min intervals; the average of the second and third measurements was used in the analysis. Blood samples were collected in the morning after fasting for at least 8 hr. FPG, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) levels were measured in a central and certified laboratory using an Advia 1650 (Siemens, Washington, DC, USA). Low-density lipoprotein cholesterol (LDL-C) was estimated indirectly using the Friedwald formula: $LDL-C = TC - (HDL-C + [TG/5])$, for subjects with TG levels < 400 mg/dL. White blood cell (WBC) was measured using an Advia 120 (Siemens).

Statistical analysis

Data are presented as mean ± SEM or %. All statistical techniques were performed using the Statistical Package for the Social Sciences for Personal Computer (SPSS, Chicago, IL, USA). ANCOVA was used to estimate BMI and WC according to FPG in each

Table 1. Age and age-adjusted characteristics according to glucose tolerance status in 1,952 Korean adult males

Parameters	FPG (mg/dL)				Diabetes	P for trend
	-89	90-99	100-109	110-125		
Number	705	675	256	133	183	
Age (yr)	44.0 ± 0.5	47.5 ± 0.5	50.4 ± 0.8	53.9 ± 1.1	56.5 ± 0.9	< 0.001
FPG (mg/dL)	83.6 ± 0.7	94.0 ± 0.7	103.9 ± 1.1	115.6 ± 1.5	154.9 ± 1.3	< 0.001
Current smoking (%)	47.1 ± 1.9	40.9 ± 1.9	35.9 ± 3.1	39.6 ± 4.3	47.7 ± 3.7	0.008
Alcohol intake (g/day)	12.8 ± 1.8	19.3 ± 1.8	18.0 ± 2.8	15.3 ± 4.0	29.5 ± 3.5	< 0.001
SBP (mmHg)	120.8 ± 0.6	122.9 ± 0.6	126.4 ± 0.9	124.4 ± 1.3	126.1 ± 1.1	< 0.001
DBP (mmHg)	79.3 ± 0.4	81.3 ± 0.4	83.8 ± 0.6	83.3 ± 0.9	82.0 ± 0.8	< 0.001
WBC (/μL)	6,625 ± 69	6,856 ± 69	6,761 ± 110	9,814 ± 160	7,420 ± 140	< 0.001
ALT (U/L)	25.2 ± 0.9	27.4 ± 0.9	37.3 ± 1.5	34.3 ± 2.1	32.3 ± 1.8	< 0.001
AST (U/L)	26.5 ± 0.7	26.2 ± 0.7	31.0 ± 1.1	31.8 ± 1.5	31.6 ± 1.3	< 0.001
LDL-C (mg/dL)	110.6 ± 1.2	116.7 ± 1.2	115.4 ± 2.0	118.9 ± 2.8	112.9 ± 2.5	0.001
HDL-C (mg/dL)	42.9 ± 0.4	42.1 ± 0.4	41.8 ± 0.6	42.7 ± 0.9	38.7 ± 0.8	< 0.001
TG (mg/dL)	139.3 ± 6.1	152.6 ± 6.2	186.7 ± 10.1	200.4 ± 14.0	277.0 ± 12.1	< 0.001
Waist circumference (cm)	82.1 ± 0.3	85.3 ± 0.3	86.7 ± 0.5	88.2 ± 0.7	87.9 ± 0.6	< 0.001
BMI (kg/m ²)	23.3 ± 0.1	24.4 ± 0.1	25.0 ± 0.2	25.2 ± 0.3	24.9 ± 0.2	< 0.001

FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; ALT, alanine transaminase; AST, aspartate transaminase; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; BMI, body mass index.

sex. Statistical significance was defined as $P < 0.05$.

Ethics statement

This study was approved by the institutional review board of the Ilsan Paik Hospital (IB-3-1107-027). After approval of study proposal, KNHANES dataset were available on the request of investigator. Because the dataset did not include any personal information and participant's consent was already taken in the process of KNHANES, our study was exempted from participant's consent by the board.

RESULTS

A total of 4,479 participants (1,952 men and 2,527 women) were analyzed. The mean BMI was $23.9 \pm 3.2 \text{ kg/m}^2$ ($24.1 \pm 3.1 \text{ kg/m}^2$

in men, $23.6 \pm 3.3 \text{ kg/m}^2$ in women).

Table 1 summarizes the data of age and age-adjusted characteristics according to glucose tolerance status in Korean adult men. Before development of diabetes, there was a progressive rise in BMI and WC according to an increase of FPG (BMI; NFG1, 23.3 ± 0.1 ; NFG2, 24.4 ± 0.1 ; IFG1, 25.0 ± 0.2 ; IFG2, 25.2 ± 0.3 ; DM, $24.9 \pm 0.2 \text{ kg/m}^2$ [P for trend < 0.001], WC; NFG1, 82.1 ± 0.3 ; NFG2, 85.3 ± 0.3 ; IFG1, 86.7 ± 0.5 ; IFG2, 88.2 ± 0.7 ; DM, $87.9 \pm 0.6 \text{ cm}$ [P for trend < 0.001]).

Table 2 summarizes the data of age and age-adjusted characteristics according to glucose tolerance status in Korean adult women. Before development of diabetes, there was a progressive rise in BMI according to an increase of FPG (BMI; NFG1, 23.0 ± 0.1 ; NFG2, 24.0 ± 0.1 ; IFG1, 24.8 ± 0.2 ; IFG2, 25.1 ± 0.4 ; DM, $24.9 \pm 0.3 \text{ kg/m}^2$ [P for trend < 0.001]). WC was increased

Table 2. Age and age-adjusted characteristics according to glucose tolerance status in 2,527 Korean adult females

Parameters	FPG (mg/dL)				Diabetes	P for trend
	-89	90-99	100-109	110-125		
Number	1,285	777	229	82	154	
Age (yr)	44.0 ± 0.4	49.7 ± 0.5	54.4 ± 0.9	55.0 ± 1.5	61.2 ± 1.0	< 0.001
FPG (mg/dL)	83.6 ± 0.3	93.6 ± 0.4	103.8 ± 0.8	116.0 ± 1.3	147.4 ± 1.0	< 0.001
Current smoking (%)	3.3 ± 0.5	3.8 ± 0.7	2.4 ± 1.2	6.7 ± 2.0	4.6 ± 1.5	NS
Alcohol intake (g/day)	2.7 ± 0.3	2.1 ± 0.4	2.8 ± 0.8	2.7 ± 1.3	3.2 ± 1.0	NS
SBP (mmHg)	115.2 ± 0.4	117.4 ± 0.5	118.8 ± 1.0	125.0 ± 1.6	122.6 ± 1.2	< 0.001
DBP (mmHg)	74.1 ± 0.3	75.6 ± 0.3	76.9 ± 0.6	78.8 ± 1.1	76.1 ± 0.8	< 0.001
WBC (μL)	$5,646 \pm 47$	$5,851 \pm 59$	$6,006 \pm 110$	$6,380 \pm 182$	$6,774 \pm 136$	< 0.001
ALT (U/L)	16.8 ± 0.3	18.0 ± 0.4	19.9 ± 0.7	19.5 ± 1.2	23.2 ± 0.9	< 0.001
AST (U/L)	22.0 ± 0.2	22.2 ± 0.3	22.1 ± 0.6	22.0 ± 0.9	22.6 ± 0.7	NS
LDL-C (mg/dL)	114.8 ± 0.8	116.4 ± 1.0	122.9 ± 1.9	122.1 ± 3.2	115.8 ± 2.5	0.001
HDL-C (mg/dL)	48.6 ± 0.3	45.8 ± 0.4	45.1 ± 0.7	45.3 ± 1.2	43.1 ± 0.9	< 0.001
TG (mg/dL)	107.4 ± 2.2	112.5 ± 2.8	129.4 ± 5.2	140.1 ± 8.7	176.9 ± 6.5	< 0.001
Waist circumference (cm)	77.1 ± 0.2	79.4 ± 0.3	81.8 ± 0.6	83.3 ± 1.0	83.7 ± 0.7	< 0.001
BMI (kg/m^2)	23.0 ± 0.1	24.0 ± 0.1	24.8 ± 0.2	25.1 ± 0.4	24.9 ± 0.3	< 0.001

FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; ALT, alanine transaminase; AST, aspartate transaminase; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; BMI, body mass index.

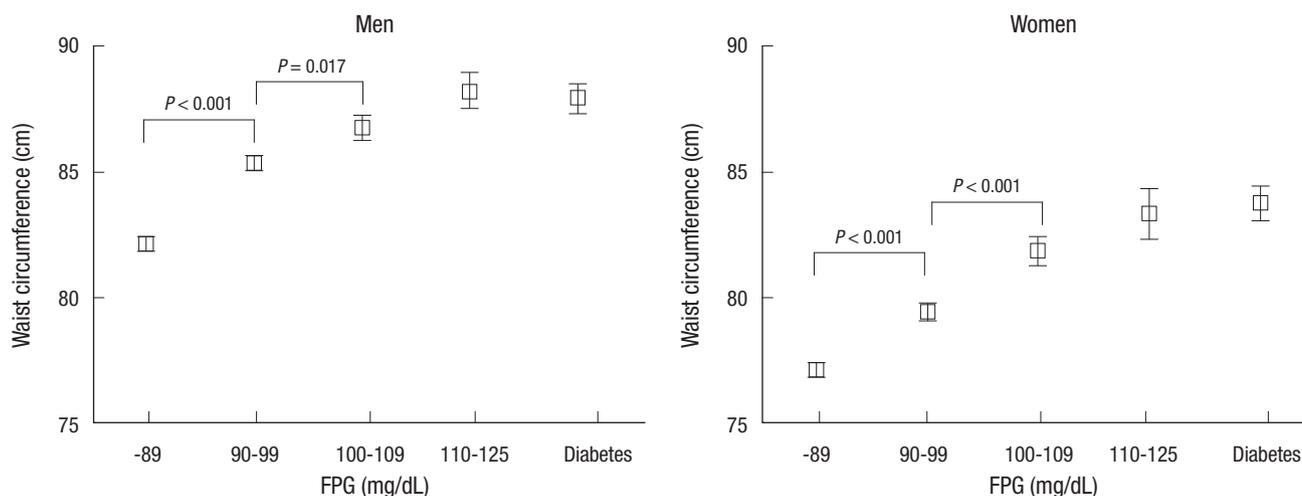


Fig. 1. Age-adjusted waist circumference according to fasting plasma glucose (FPG). Diabetes was defined as current medication of anti-diabetes or FPG $\geq 126 \text{ mg/dL}$. Data, mean \pm SEM.

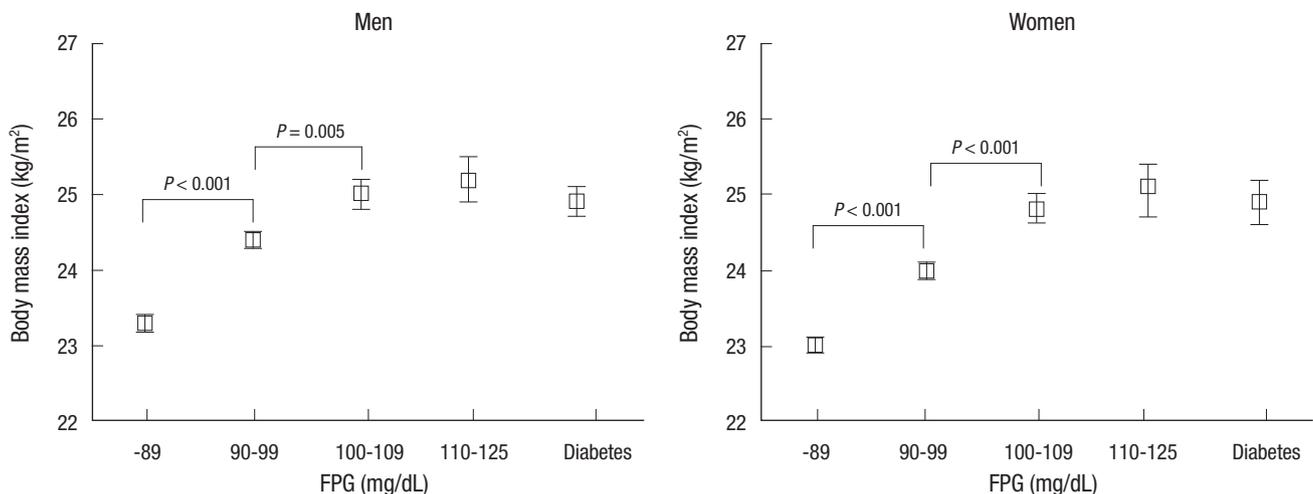


Fig. 2. Age-adjusted body mass index according to fasting plasma glucose (FPG). Diabetes was defined as current medication of anti-diabetes or FPG \geq 126 mg/dL. Data, mean \pm SEM.

according to an increase of FPG (WC; NFG1, 77.1 ± 0.2 ; NFG2, 79.4 ± 0.3 ; IFG1, 81.8 ± 0.6 ; IFG2, 83.3 ± 1.0 ; DM, 83.7 ± 0.7 cm [P for trend < 0.001]).

Fig. 1 depicts results of age-adjusted WC according to FPG and diabetes. In men, age-adjusted WC of NFG2 was significantly higher compared to that of NFG1 ($P < 0.001$) and age-adjusted WC of IFG1 was significantly higher compared to that of NFG2 ($P = 0.017$). Similar results were observed in women (WC of NFG2 vs NFG1, $P < 0.001$; IFG1 vs NFG2, $P < 0.001$). In each sex, there was no further increase of WC with increase of FPG in IFG1, IFG2, and DM.

Fig. 2 depicts age-adjusted BMI according to FPG and diabetes. In men, age-adjusted BMI of NFG2 was significantly higher compared to that of NFG1 ($P < 0.001$) and age-adjusted BMI of IFG1 was significantly higher compared to that of NFG2 ($P = 0.005$). The similar results were observed in women (BMI of NFG2 vs NFG1, $P < 0.001$; IFG1 vs NFG2, $P = 0.001$). In each sex, there was no further increase of BMI with increase of FPG in IFG1, IFG2, and DM.

DISCUSSION

As far as we know, this is the first study about in which stage of glucose intolerance persons showed a maximum obesity in Korean general population. The data suggested that degree of obesity increased with an increase of FPG in range of FPG < 100 mg/dL, peaked in FPG of 100-109 mg/dL, and then plateaued in higher FPG range in general Korean population. Contrary to our results, many Western studies showed that before development of diabetes, body weight increases progressively, reaching a maximum at the time of diagnosis, and then it tends to decrease after diagnosis (6, 15-21). Considering this is an only cross-sectional study to observe the association of obesity with degree of glucose intolerance, we could not confirm this result without

further longitudinal follow-up study. However, this result suggested different relationship between obesity and glucose intolerance in Korean population, compared to Western population.

It was well-known that obesity contributes to the development of T2DM (1-3) and weight control efforts are an important component of the clinical management of diabetes (4, 5). The association between obesity and diabetes is indisputable (6, 15-21). A meta-analysis presented the overall relative risk of diabetes per unit of BMI and reported that diabetes risk increases by 1.19 (95% CI:1.16-1.20) per unit of BMI and assumes a linear relation between BMI and the relative risk of diabetes (2). In our study, BMI and WC was associated with the presence of diabetes (FPG ≥ 126 mg/dL or those with diabetes drug) independent of age, sex, current smoking, alcohol intake, systolic and diastolic blood pressure, LDL-cholesterol, triglyceride, and HDL-cholesterol, respectively (BMI, OR 1.095 [95% CI:1.047-1.145], $P < 0.001$ per unit of BMI; WC, OR 1.049 [95% CI 1.032-1.067], $P < 0.001$ per unit of WC) in logistic regression analysis.

A study involving Pima Indians reported a steady gain in weight before the diagnosis of diabetes (mean BMI increase of 0.43-0.71 kg/m² per year), with weight declining following diagnosis (15). On the contrary that almost all Western studies consistently showed that body weight reached a maximum at the time of diagnosis on type 2 diabetes (6, 15-18), we could not observe those findings in this study. Previously, we examined the medical records of 54,623 persons who attended a health promotion center and observed that BMI increased gradually with an increase of FPG in the range of NFG and IFG. However, we could not find difference of obesity between IFG and diabetes (26). Oh et al. analyzed NFG and IFG population according to FPG level, as follows: NFG (< 100 mg/dL), stage 1 IFG (100-109 mg/dL) and stage 2 IFG (110-125 mg/dL) in a pooled analysis of four community-based cohort studies in Korea, which was conducted by the Committee of the Korean Diabetes Associa-

tion on the diagnosis and classification of diabetes mellitus (29). Although the main purpose of that study was whether stage 2 IFG was poorer metabolic profile or not compared to IFG 1, BMI and WC in stage 2 IFG were significantly higher than those in stage 1 IFG, respectively (BMI, 24.6 ± 3.2 kg/m² vs 23.8 ± 3.3 kg/m²; WC, 86.8 ± 8.6 cm vs 83.9 ± 9.5 cm) on the contrary to our results. The reason of this discrepancy is not certain. One of possibility was the difference in characteristics of study population. Because major population of pooled analysis was originated from Korean rural area (Yonchon and Chongup), mean age of the pooled study was higher than that of our NFG and IFG participants (pooled analysis, 52.1 ± 13.6 yr vs our study 48.0 ± 14.0 yr), nevertheless our study included only participants older than 25 yr. Another explanation could be difference of exclusion criteria. On the contrary that the pooled study included whole population of four communities, we included only participants older than 25 yr for excluding the possibilities of type 1 DM and excluded participants with history of cancer, cerebrovascular disease, end stage renal disease, liver cirrhosis, and thyroid disease, which may cause its effect on weight. Among 5,531 persons with laboratory test and nutritional survey data, 4,479 persons aged 26-99 yr were included as participants according to above mentioned inclusion criteria.

According to analysis of the 1999-2006 National Health and Nutrition Examination Survey in the United States (28), 80.3% of adult diabetics were considered overweight (BMI ≥ 25 kg/m²) and 49.1% of diabetics were considered obese (BMI ≥ 30 kg/m²). In 2001 KNHANES (29), the rate of BMI ≥ 25 kg/m² was 48.4% and the rate of BMI ≥ 30 kg/m² was 7.4% in diabetics. Lee et al. investigated 15,665 Korean diabetic subjects and found that 67.6% had a BMI below 25 kg/m², and only 3.3% had a BMI over 30 kg/m². Their study showed that the majority of Korean diabetics were non-obese and suggested the etiologic difference of type 2 diabetes in Korean subjects compared to Caucasians (30). The prevalence of type 2 diabetes among the second-generation Japanese-Americans is even 2- to 4-fold higher than that among western populations despite the fact that the second-generation Japanese-Americans are less obese than the Caucasians (31). The finding in our study that degree of obesity increased with an increase of FPG in range of FPG < 100 mg/dL, peaked in FPG of 100-109 mg/dL, and then plateaued in higher FPG range was comparable with above mentioned studies. These findings may imply that East Asians are more prone to develop diabetes for their degree of obesity.

Both insulin deficiency and insulin resistance have been known to be involved in the pathogenesis of type 2 diabetes. Weyer et al. showed that the inability of insulin secretion to compensate for the increase in insulin resistance distinguishes individuals who will develop diabetes from those who will retain NGT in Pima Indians (32). The relative importance of each factor may differ according to ethnicity. In previous study (12), we classi-

fied our 370 participants according to glucose intolerance into five groups (normal glucose, isolated IFG, isolated IGT, both IFG and IGT, and diabetes) after 75 g oral glucose tolerance test (OGTT). And we compared insulinogenic index (Δ insulin, 0 to 30 min/ Δ plasma glucose, 0-30 min; an index of early-phase insulin secretion during the OGTT) (33) and HOMA (R) (fasting serum insulin [μ U/mL] \times FPG [mM/L]/22.5; an index of insulin resistance) (34) among five groups. In that study, insulinogenic index significantly decreased in subjects with isolated IFG and isolated IGT compared to normal glucose but there was no difference in HOMA (R) among those with isolated IFG, isolated IGT, and normal glucose. This finding that insulinogenic index was the sole differentia among normal glucose, isolated IFG, and isolated IGT suggested the importance of early-phase insulin secretory defect in the pathogenesis of type 2 diabetes in Korea. The uniqueness of this study was that degree of obesity increased gradually with an increase of FPG, peaked in FPG of 100-109 mg/dL, but no more increase of obesity in higher FPG range. There was no significant difference of obesity among FPG of 100-109 mg/dL (stage 1 IFG), FPG of 110-125 mg/dL (stage 2 IFG), and diabetes. This finding implied that even in mild or stage 1 IFG, persons already reached their maximum obesity in the course of glucose tolerance deterioration in Korea. With this result, we can speculate that failure of insulin secretion to compensate obesity-induced insulin resistance may be initiated in stage 1 IFG in Korean population. However, we should consider that this is not a longitudinal follow-up study for the same person's weight but a cross-sectional observation of different person's weight. Another study is necessary to confirm the suggestion of this study.

The study had several limitations. The first was that this was not a longitudinal follow-up for a participant's weight change, but was rather a cross-sectional observation for the association of obesity with glucose tolerance state. The second was that we could not adjust the effect of treatment of diabetes including oral anti-diabetic drug and insulin for the association of obesity with glucose tolerance state. The strength of this study was that it was conducted based on nationally representative data of the civilian, non-institutionalized Korean population. As far as we know, this is the first study about the association of obesity and glucose intolerance status in a representative population of Koreans.

In conclusion, we observed that BMI and WC were increased progressively according to glucose intolerance status before development of diabetes in both males and females. The degree of obesity increases with increasing FPG in the NFG range, peaks in FPG of 100-109 mg/dL, and then plateaus in higher FPG range. Although this is only cross-sectional observation, this finding can be a clue for proper direction of further prospective studies and proper strategies for diabetes prevention in Korea.

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