Int J Diabetes Dev Ctries (April–June 2012) 32(2):75–81
DOI 10.1007/s13410-012-0069-z

ORIGINAL ARTICLE

Potential effect of insulin resistance and cardiovascular risk factors on metabolic syndrome in subjects with normal fasting plasma glucose levels

Dong Wook Jeong · Jeong Gyu Lee · Sangyeoup Lee · Yun Jin Kim · Jae Ho Bae · Dong Hee Kim · Yu Hyeon Yi · Young Hye Cho · Uisoo Chae

Received: 13 April 2011 / Accepted: 16 April 2012 / Published online: 12 May 2012

Abstract The prevalence of metabolic syndrome has progressively increased with increasing fasting plasma glucose (FPG) levels. This study aimed to investigate the influence of insulin resistance and cardiovascular risk factors on metabolic syndrome in individuals with normal FPG. Study subjects with FPG levels below 100 mg/dL were divided into 5 groups depending on the exact FPG levels. We then evaluated the association of metabolic syndrome with insulin resistance and total cholesterol/ high density lipoprotein-cholesterol ratio (TC/HDL ratio). The odds ratio of insulin resistance in the level of HOMA-IR above 2.34 group [3.483(95 % CI, 1.110~10.932)] was significantly increased in the group of FPG level from 93 mg/dL to 99 mg/dL compared to the group below 80 mg/dL. The odds ratio of metabolic syndrome in the group of FPG level from 89 mg/dL to 92 mg/dL [2.459, (95%CI, 1.275~4.741)] and 93 mg/dL to 99 mg/dL [2.079, (95%CI, 1.052~4.110)] was significantly increased compared to the group below 80 mg/dL after adjusting age, sex, smoking status, physical activity, heavy drinking, TC/HDL ratio. Higher FPG levels within the normoglycemic range may constitute a risk of insulin resistance and is associated more strongly with the risks of metabolic syndrome.

Keywords Blood glucose · Metabolic syndrome · Insulin resistance · Cholesterol · Glucose intolerance

D. W. Jeong · J. G. Lee (✉) · S. Lee · Y. J. Kim · Y. H. Yi · Y. H. Cho
Center for Obesity, Nutrition and Metabolism,
Department of Family Medicine and Medical Research Institute,
Pusan National University School of Medicine,
Pusan National University Hospital,
1-10 Ami-dong, Seo-gu,
Busan 602-739, South Korea
e-mail: jeklee@pusan.ac.kr

S. Lee
Medical Education Unit,
Pusan National University School of Medicine,
Busan, South Korea

J. H. Bae
Department of Biochemistry,
Pusan National University School of Medicine,
Busan, South Korea

D. H. Kim
College of Nursing, Pusan National University,
Busan, South Korea

U. Chae
Pusan National University School of Medicine,
Busan, South Korea

Introduction

During 1997–2003, the American Diabetes Association (ADA) proposed Fasting Plasma Glucose (FPG) levels ranging between 110 and 125 mg/dL as indicative of impaired fasting glucose [1]. In 2003, the ADA further modified diagnostic criteria defining FPG levels <100–109 mg/dL as being abnormal [2]. Although there have been several counter arguments against this criteria [3–5], these lower FPG levels were defined because disorder in FPG levels are associated with a high prevalence of diabetes [6]. Further, disorders in FPG are closely related to a high occurrence of risk factors of cardiovascular disease, such as dyslipidemia and hypertension [7, 8]. Recently, metabolic syndrome has been introduced as a multifaceted syndrome responsible for hypertension, abnormalities of glycometabolism,

dyslipidemia and obesity. New diagnostic criteria for metabolic syndrome, using the new criteria [2] of disorders in FPG, have been proposed by the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) [9]. Thus, FPG levels that were once regarded to be within the normal range are now considered abnormal. Such higher FPG levels are considered to indicate impaired fasting glucose (IFG). Many studies have revealed that metabolic risk factors increase with elevations in FPG levels within the normal range and that such patients are prone to developing insulin resistance, which leads to type 2 diabetes [10, 11]. That is, although FPG levels are within the normal range, the risk of metabolic syndrome increases if the FPG level is even slightly elevated. However, few studies have assessed the effects of insulin resistance and the risk factors of cardiovascular disease on metabolic syndrome in subjects with normal FBG level. In this study, therefore, we investigated the influence of insulin resistance on metabolic syndrome by using Homeostatic model assessment-insulin resistance (HOMA-IR) [12, 13] and Quantitative insulin sensitivity check index (QUICKI) [14] as also evaluating cardiovascular risk factors in individuals by measuring total cholesterol, HDL-cholesterol, and total cholesterol/ HDL-cholesterol ratio (TC/HDL ratio) [15].

Materials and methods

Subjects

Our study sample comprised individuals who visited the Health Promotion Center of the University hospitals in Pusan for medical examination from January to December 2007. Among them, 3,207 participated in this study. Our exclusion criteria were as follows: AST and ALT levels exceeding more than twice of the normal value (i.e., 80 units per liter), abnormal values of FT_4 and TSH, individuals currently being treated with diabetes medication, individuals taking medication for dyslipidemia, individuals whose level of insulin could not be measured, and individuals whose habits, such as exercise, smoking, and alcohol consumption, were not examined. These subjects were divided into four groups based on gender and age (30–39, 40–49, 50–59, and 60–69 years old) according to the 2005 census conducted by the National Statistical Office [16]. Then, we randomly selected 1,505 individuals with regard to the population proportions from the census for appropriate calibration. Eventually, 1,307 individuals whose blood FPG levels were normal (lower than 99 mg/dL) were included in this study. Individuals in the age group of 15–29 years and over 70 years were excluded because of very low frequency of visits. All participants gave informed consent and this study was approved by the Institutional Review Board at Pusan National University Hospital.

Measurements

The subjects were examined in terms of the present illness, past history, and habits of drinking alcohol and smoking. Height and weight were measured to 0.1 cm and 0.1 kg, respectively, by electronic medical instruments, HM-300 (Fanics Co. Ltd., Busan, South Korea) while the subjects wore a light dressing gown. Body mass index (BMI, kg/m^2) was calculated based upon the measured height and weight. Systolic and diastolic blood pressure was recorded once using an automatic blood pressure machine (BP-203 RVII Colin Corp., Aichi, Japan). According to the guidelines of the World Health Organization (WHO), the abdominal circumference was directly measured at slimmest section between the lowest ribs and the iliac crest and recorded to 0.1 cm accuracy in the inspiration phase. We performed the following laboratory blood tests after 8 h of fasting. Total Cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C). The liver enzyme GGT were measured by enzymatic colorimetric method with Hitachi 7600 chemical analyzer (Hitachi co., Ltd, Tokyo, Japan). The mean intra-assay and inter-assay coefficients of variation (CV) values were as follows; (Total cholesterol, 0.8 and 0.7 %), (LDL-C, 1.4 and 0.6 %), (HDL-C, 1.2 and 0.4 %), respectively. Triglycerides were measured by using lipase, glycerol kinase (GK), glycerol phosphate oxidase (GPO), peroxidase (POD) with glycerol blank. The mean intra-assay and inter-assay CV values were 0.9 and 1.1 %, respectively. FPG was measured by the glucose oxidase method (LX-20, Beckman Coulter, USA). The mean intra-assay and inter-assay CV values were 1.3 and 0.6 %, respectively. Plasma insulin level was measured by solid-phase ^{125}I radioimmunoassay with Coat-A-Count® Insulin. The mean intra-assay and inter-assay CV values were 4.2 and 6.3 %, respectively. Thyroid stimulating hormone (TSH) was measured by Coat-A-Count TSH IRMA (Siemens Los Angeles, CA, USA), while Free T4 (FT_4) was measured by Coat-A-Count Free T4 (Siemens Los Angeles, CA, USA).

Using a medical questionnaire, we examined lifestyle factors such as drinking, smoking, and exercise. For alcohol consumption, (1 drink=14 g of alcohol), excessive drinking was defined as follows: for males ≥14 drinks/week (alcohol, 196 g) and for females and elderly individuals ≥7 drinks or more/week (alcohol, 98 g). This included the consumption of beer, whiskey, and/or rice wine based on the guidelines of the National Institute Alcohol Abuse and Alcoholism [14]. For smoking, we categorized non-smokers as those who had never smoked as well as those who had now quit smoking. Smokers were individuals who smoked currently. With regard to exercise, the high-exercise group comprised individuals who exercised for more than 20 minutes at a time, three times a week or more. This was determined after observing the time and frequency of exercise for a week.

Cardiovascular risk factor

Total blood cholesterol, HDL-cholesterol and TC/HDL ratio [17, 18] values were measured and compared. The TC/HDL ratio is highly correlated to coronary heart disease if the ratio exceeds 4.5. The American Heart Association (AHA) recommends maintaining this ratio ≤3.5 [19]. Therefore, a ratio greater than 3.5 was considered abnormal in this study.

Insulin resistance

HOMA-IR- a well known index of insulin resistance-and QUICKI-a quantitative standard for insulin sensitivity-were calculated by using the following formulae: [HOMA-IR = fasting plasma insulin (μU/mL) × FPG (mg/dL) / 22.5× 18.182] [13], QUICKI = 1/[log fasting insulin(μU/mL) + log FPG(mg/dL)] [14]. The cutoff values for defining insulin resistance was HOMA-IR=2.34 and QUICKI=0.33 [20].

Definition of metabolic syndrome

We used the 2005 American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria for the diagnosis of metabolic syndrome [9, 21]. We defined central obesity as a waist circumference ≥90 cm in males and ≥85 cm in females, according to geography-specific cut points for waist circumference [22].

Of the following 5 criteria, metabolic syndrome is diagnosed if at least three criteria are satisfied.

(1) Waist measurement ≥90 cm (men), ≥85 cm (women)
(2) Blood pressure ≥130/85 mmHg or individuals taking antihypertensive drugs
(3) FPG ≥100 mg/dL or individuals being treated for diabetes mellitus
(4) Triglycerides ≥150 mg/dL or individuals being treated for dyslipidemia
(5) HDL Cholesterol <40 mg/dL (men), <50 mg/dL (women) or individuals being treated for dyslipidemia

Statistical analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, Inc., Chicago, USA) version 12.0 for windows. The general and biochemical characteristics of the subjects according to gender were compared using an independent sample *T*-test. Study subjects were evenly divided into five quintiles (Q1 ≤80 mg/dL, 81 ≦ Q2 ≦ 84 mg/dL, 85 ≦ Q3 ≦ 88 mg/dL, 89 ≦ Q4 ≦ 92 mg/dL, 93 ≦ Q5 ≦ 99 mg/dL) depending on the percentile for FPG <100 mg/dL. In five multivariate models according to the FPG subgroup, we performed linear and linear trend analysis using the chi-square test for abdominal obesity, high triglyceride, LDL-cholesterol, high blood pressure, obesity based on the BMI, and multiple life factors, such as smoking status, alcohol consumption, and exercise. In the multivariate model, a cross ratio of each FPG sub-type and 95 % confidence intervals was compared by using logistic regression analysis for metabolic syndrome, insulin resistance, decreased insulin sensitivity, and high cardiovascular risk factors. Assessments were performed after adjusting for age and gender, multiple life factors such as smoking, drinking and exercise status. Insulin resistance was analyzed by calibrating abdominal circumference and BMI. Cardiovascular risk factors were eventually analyzed by calibrating insulin resistance. A *P*-value less than 0.05 was deemed statistically significant. All statistical tests were two-sided.

Results

Characteristics of study subjects

Our study sample comprised 678 men and 629 women. There were no significant differences for age and total cholesterol based on gender. However, significant differences were noted for FPG levels, BMI, systolic blood pressure, diastolic blood pressure, triglycerides, LDL-cholesterol, HDL-cholesterol, TC/ HDL-cholesterol ratio, HOMA-IR, and QUICKI values between men and women ($p<0.001$) (Table 1).

Table 1 Baseline characteristics of study subjects by gender[a]

Variables	Men (*N*=678)	Women (*N*=629)	*p*-value
Age (years)	45.7±9.9	46.3±10.0	0.226
Fasting plasma glucose (mg/dL)	87±7	85±7	<0.001
BMI (kg/m^2)	24.5±2.6	23.2±2.7	<0.001
Systolic BP (mmHg)	123±16	116±16	<0.001
Diastolic BP (mmHg)	76±10	71±10	<0.001
Total cholesterol (mg/dL)	194±33	191±34	0.068
Triglyceride (mg/dL)	140±81	98±78	<0.001
HDL cholesterol (mg/dL)	51±13	63±15	<0.001
LDL cholesterol (mg/dL)	125±29	117±31	<0.001
TC/HDL ratio	3.97±1.08	3.21±0.96	<0.001
HOMA-IR	1.17±0.63	0.98±0.61	<0.001
QUICKI	0.39±0.04	0.40±0.06	<0.001

[a] Plus-minus values are represented as mean ± SD. p value by two sample *t*-test between men and women. *BMI* Body Mass Index, *BP* Blood Pressure, *HDL* High-Density Lipoprotein, *LDL* Low-Density Lipoprotein, *TC/HDL* Total Cholesterol/High-Density Lipoprotein cholesterol, *HOMA-IR* Homeostatic Model Assessment-Insulin Resistance, *QUICKI* Quantitative Insulin Sensitivity Check Index

Relationship between metabolic risk factors and lifestyle factors based on FPG levels

Regarding metabolic risk factors and lifestyle factors for the five normal FPG level groups statistically significant increases were noted for the prevalence rate of abdominal obesity, hypertriglyceridemia, high blood pressure, obesity based on BMI and excessive drinking from Q1 to Q5 ($p<0.001$); moreover, the prevalence rate for non-smoking and smoking was also significantly increased ($p=0.001$). However, no statistically significant difference was noted for LDL-cholesterol levels and exercise status (Table 2).

Total cholesterol and TC/HDL ratio increased with increasing FPG levels

On comparing the lipid profiles for the increasing quintiles of FPG levels, significant increases in the total cholesterol level were noted ($P<0.001$). Further, the prevalence rate for cardiovascular risk (TC/HDL ratio >3.5) also demonstrated a statistically significant increase from Q1 to Q5 ($P<0.001$, $p=0.008$) (Table 2).

Insulin resistance increased with increasing FPG levels

The prevalence rate of insulin resistance for the five groups of FPG levels was evaluated using both the parameters of HOMA-IR >2.34 and QUICKI <0.33; a statistically significant increase was noted from Q1 to Q5 ($p<0.001$). Further, HOMA-IR showed a tendency to increased odds ratio values with FPG levels as compared to group Q1. The values for groups Q4 and Q5 were statistically significant, and the odds ratio remained high after adjusting for age, gender, and lifestyle factors. However, after adjusting BMI and abdominal circumference, only group Q5 showed a significantly high odds ratio of 3.483(95 % CI, 1.110–10.932) (Table 3). QUICKI showed tendencies similar to those noted for HOMA-IR; only the odds ratio for group Q5 [5.374, (95 % CI, 1.146–25.202)] was statistically significant after adjusting for age, gender, lifestyle factor, BMI, and abdominal circumference (Table 3).

Increasing prevalence of metabolic syndrome with increasing FPG levels

The prevalence rate of metabolic syndrome showed a tendency to increase as follows: 5.2 %, 8.3 %, 9.4 %, 16.2 %, and 13.1 % from Q1 to Q5, and this was statistically significant ($p<0.001$). The odds ratios for Q2, Q3, Q4, and Q5 groups were all high as compared to group Q1 for metabolic syndrome; however, Q4 (OR=2.935, 95 %CI 1.557–5.534, $p=0.001$) and Q5 (OR=2.282, 95 %CI 1.188–4.383, $p=0.013$) were statistically significant. Q4 (OR=2.899, 95 %CI 1.531–5.490, $p=0.001$) and Q5 (OR=2.485, 95 %CI 1.128–4.233, $p=0.021$) were statistically significant even after adjusting for gender, age, and lifestyle factors. However, the odds ratio of other groups, except Q4 (OR=2.507, 95 %CI 1.310–4.799, $p=0.006$) were not statistically significant after adjusting for insulin resistance (Table 3).

Table 2 Metabolic and lifestyle factors according to the quintiles of normal fasting plasma glucose levels

Variables	Fasting Plasma Glucose (FPG) level					*p*-value[a]
	Q1	Q2	Q3	Q4	Q5	
N (numbers)	286	264	286	235	236	
Mean values of FPG (mg/dL)	76.6	82.5	86.5	90.4	95.6	
Range of FPG (mg/dL)	≤80	81–84	85–88	89–92	93–99	
Male gender (%)	42.3	46.2	49.7	61.3	63.1	
Abdominal obesity (%)[c]	18.9	24.2	28.0	34.9	32.6	<0.001
Triglyceride ≥150 mg/dL (%)	15.0	17.0	22.4	31.9	31.8	<0.001
Low HDL (%)[d]	17.5	17.4	14.7	19.6	17.4	0.826
BP ≥130/85 mmHg (%)	16.8	22.3	29.0	31.5	37.7	<0.001
BMI ≥25 kg/m^2 (%)	23.4	27.3	36.4	40.9	45.8	<0.01
Mean values of TC (mg/dL)	190.0	191.0	191.6	194.5	196.6	<0.001[b]
Mean values of HDL-C (mg/dL)	58.9	57.9	57.9	52.8	55.6	<0.001[b]
TC/HDL ratio ≥3.5 (%)	41.3	42.4	45.1	59.6	52.5	<0.001
Smoking status						
Past (%)	13.3	18.2	22.4	26.4	30.5	<0.01
Current (%)	25.9	20.1	20.3	24.7	27.5	<0.01
Heavy drinking (%)[e]	15.4	17.0	22.1	26.4	35.7	<0.001
High physical activity (%)[f]	81.8	81.8	82.2	83.4	82.2	0.753

[a]By linear association, [b]By One way ANOVA, [c]The Asia Pacific abdominal obesity criterion (waist circumference >90 cm in men, >85 cm in women) was used, [d]Low high-density lipoprotein cholesterol <40 mg/dL for men, <50 mg/dL for women, *TC/HDL*: Total Cholesterol/High-Density Lipoprotein, *BP*: Blood Pressure, *BMI*: Body Mass Index, [e]Heavy drinking denotes consumption of 14 or more drinks per week for men and 7 or more drinks per week for women, [f]physical activity denotes engagement in physical activity for a minimum of 20 min at least three times per week

Table 3 Prevalence and odds ratio for insulin resistance according to the quintiles of normal fasting plasma glucose levels

Variables	Fasting plasma glucose level				
	Q1	Q2	Q3	Q4	Q5
FPG (mg/dL)	≤80	81–84	85–88	89–92	93–99
Insulin resistance (%)[a]	1.4	1.5	3.5	6.8	7.6
OR (95 % CI)	1[Reference]	1.09(0.27–4.38)	2.55(0.79–8.24)	5.15(1.70–15.63)	5.82(1.94–17.45)
Adjusted OR (95 % CI)					
Model 1[b]	1[Reference]	1.06(0.26–4.30)	2.40(0.74–7.77)	4.54(1.48–13.91)	5.15(1.70–15.58)
Model 2[c]	1[Reference]	1.04(0.26–4.20)	2.38(0.73–7.76)	4.50(1.46–13.86)	5.17(1.69–15.84)
Model 3[d]	1[Reference]	0.87(0.21–3.61)	1.72(0.52–5.75)	3.08(0.98–9.69)	3.48(1.11–10.93)
Low Insulin sensitivity(%)[e]	0.7	1.1	2.8	4.3	5.1
OR(95 % CI)	1[Reference]	1.63(0.27–9.85)	4.09(0.86–19.41)	6.31(1.37–29.09)	7.61(1.69–34.34)
Adjusted OR (95 % CI)					
Model 1[b]	1[Reference]	1.62(0.27–9.76)	3.90(0.82–18.60)	5.77(1.24–26.86)	7.05(1.55–32.14)
Model 2[c]	1[Reference]	1.56(0.26–9.76)	3.90(0.81–18.71)	5.66(1.21–26.54)	7.41(1.60–34.26)
Model 3[d]	1[Reference]	1.33(0.22–8.16)	3.01(0.61–14.69)	3.99(0.90–20.83)	5.37(1.15–25.20)
Metabolic syndrome(%)[f]	5.2	8.3	9.4	16.2	13.1
OR(95 % CI)	1[Reference]	1.64(0.83–3.24)	1.88(0.98–3.62)	3.49(1.87–6.51)	2.73(1.44–5.20)
Adjusted OR (95 % CI)					
Model 1[b]	1[Reference]	1.61(0.82–3.20)	1.75(0.91–3.39)	2.94(1.56–5.53)	2.28(1.19–4.38)
Model 2[c]	1[Reference]	1.62(0.81–3.20)	1.74(0.90–3.38)	2.90(1.53–5.49)	2.49(1.13–4.23)
Model 4[g]	1[Reference]	1.62(0.81–3.23)	1.63(0.83–3.19)	2.51(1.31–4.80)	1.80(0.91–3.54)

CI: Confidence Interval, *FPG*: Fasting Plasma Glucose, *OR*: Odds Ratio, [a] $p<0.001$ by likelihood test for trend, Insulin resistance: Homeostatic model assessment-insulin resistance ≥2.34, [e] $p<0.001$ by likelihood test for trend, Low insulin sensitivity; Quantitative insulin sensitivity check index ≤0.33, [f] $P<0.001$ by likelihood test for trend, metabolic syndrome is defined by 2005 American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) criteria

[b] Model 1 is adjusted for age and sex

[c] Model 2 is adjusted for age, sex, smoking status (never smoker, past smoker, current smoker), physical activity (a minimum of 20 min at least three times per week), and heavy drinking(14 or more drinks per week for men and 7 or more drinks per week for women)

[d] Model 3 is adjusted for age, sex, smoking status, physical activity, heavy drinking, body mass index, and waist circumference

[g] Model 4 is adjusted for age, sex, smoking status, physical activity, heavy drinking, and insulin resistance

Discussion

In this study, adults without diabetes and with normal FPG levels showed a tendency toward increased insulin resistance and TC/HDL ratio with increasing FPG levels, along with an increasing odds ratio. In insulin-resistance, HOMA-IR and QUICKI both showed statistically significant increases in groups for which the FPG level was the highest as compared to groups for which the odds ratio is the lowest. This supports a recent study that specified that FPG criteria could be set to less than 100 mg/dL for predicting the occurrence of type 2 diabetes.

One prospective study revealed that insulin resistance demonstrated an increasing tendency in people with normal FPG levels but with higher metabolic risk factors [18]. Further, in a recent research higher fasting plasma glucose levels within the normoglycemic range constitute an independent risk factor for type 2 diabetes among young men [10]. For our research, the prevalence of metabolic syndrome increased according to FPG levels. But 4th quintile has more abdominal obesity and highest prevalence of metabolic syndrome. We calculated the odds ratio of metabolic syndrome according to increased FPG levels and complemented this calculation with insulin resistance and evaluated its effect on metabolic syndrome. As a result, the odds ratio showed a statistically significant increase only in group Q4, with no statistical significance for other groups, suggesting that insulin resistance has a significant effect in causing metabolic syndrome even in individuals with normal FPG levels.

Meanwhile, TC/HDL ratio does not have a definite effect on calibrated odds ratio of metabolic syndrome, insulin resistance may plays more important role on metabolic syndrome than lipid profile. Q4 showed a higher value of the TC/HDL ratio than the other groups, may have contributed to the statistically high odds ratio of metabolic syndrome for calibrated insulin resistance. However, the differences between the five groups with normal FPG levels suggests that further research is required to determine the normal FPG range. It has been mentioned that the criteria need to be lowered to below

100 mg/dL in order to predict type 2 diabetes, although recently, the lower limit of impaired fasting glucose has been changed to 100 mg/dL [23, 24]. Higher FPG level is well known to be a continuous risk for diabetes and cardiovascular disease. Dysglycemia refers to this continuous risk just like serum lipid levels [25]. Another report also observed that a higher but normal FPG level was related to a high-sensitivity C-reactive protein (hsCRP); this report corresponded with all of our other findings [26]. Insulin resistance has been reported as an important risk factor for BMI and abdominal circumference in adults [27]. We consider that greater attention is required for treating insulin resistance, which is critical in causing metabolic syndrome.

This study has several limitations. It is not a prospective but a cross-sectional study, which does not reflect the laboratory data of the age group of 20's and 70's; it is therefore difficult to generalize the results of this research. Further, because the normal FPG group was classified by only one laboratory result, there is a possibility that the group may include patients of diabetes or impaired glucose tolerance; these can be eliminated by oral glucose tolerance test or HbA1c levels. The third is that among several cardiovascular risk factors, only the TC/HDL ratio was considered, again limiting the generalization of our results. The fourth is that blood pressure was recorded only once. Lastly, it is yet to be seen whether our results can be generalized to other ethnic groups because the present study was conducted exclusively in the Korean adults.

The advantage of this study is that unlike the other studies, we significantly lowered the error because the selection of samples was based on the population proportion from the census; moreover, due to the exclusion of data of patients with diabetes, the bias caused by patients with diabetes under treatment could be significantly calibrated. Also, another strength of this research is that information regarding metabolic syndrome in normal FPG level individuals and the relationship between cardiovascular risk factors and metabolic syndrome is not yet sufficient.

In conclusion, by studying the effect of insulin resistance on the prevalence of metabolic syndrome and the effect of management of insulin resistance through further research, the criteria for treatment need to be determined in order to clarify whether the treatment for people with insulin resistance within the normal FPG range is beneficial.

Conflict of interest There are no conflicts of interest.

References

1. American Diabetes Association. Standards of medical care in diabetes-2007. Diab Care. 2007;30:S4–S41.
2. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Expert Committee on the Diagnosis and Classification of Diab Mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diab Care. 2003;26:3160–7.
3. Genuth S. Lowering the criterion for impaired fasting glucose is in order. Diab Care. 2003;26:3331–2.
4. Borch-Johnsen K, Colagiuri S, Balkau B, Glumer C, Carstensen B, Ramachandran A, et al. Creating a pandemic of prediabetes: the proposed new diagnostic criteria for impaired fasting glycaemia. Diabetologia. 2004;47:1396–402.
5. Schriger DL, Lorber B. Lowering the cut point for impaired fasting glucose: where is the evidence? Where is the logic? Diab Care. 2004;27:592–601.
6. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, et al. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diab Care. 2007;30:753–9.
7. Despres JP, Lamarche B, Mauriege P, Cantin B, Dagenais GR, Moorjani S, et al. Hyperinsulinemia as an independent risk factor for ischemic heart disease. N Engl J Med. 1996;334:952–7.
8. Sattar N, Williams K, Sniderman AD, D'Agostino R, Haffner SM. Non-high-density lipoprotein cholesterol with other cardiovascular risk factors in patients with the metabolic syndrome in the insulin resistance atherosclerosis study. Circulation. 2004;110:2687–93.
9. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112:2735–52.
10. Tirosh A, Shai I, Tekes-Manova D, Israeli E, Pereg D, Shochat T, et al. Israeli Diabetes Research Group. Normal fasting plasma glucose levels and type 2 diabetes in young men. N Engl J Med. 2005;353:1454–62.
11. Thomas GN, Chook P, Qiao M, Huang XS, Leong HC, Celermajer DS, et al. Deleterious impact of "high normal" glucose levels and other metabolic syndrome components on arterial endothelial function and intima-media thickness in apparently healthy Chinese subjects: the CATHAY study. Arterioscler Thromb Vasc Biol. 2004;24:739–43.
12. Bonora E, Targher G, Alberiche M, Bonadonna RC, Saggiani F, Zenere MB, et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity. Diab Care. 2000;23:57–63.
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentration in man. Diabetologia. 1985;28:412–9.
14. Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab. 2000;85:2402–10.
15. Lemieux I, Lamarche B, Couillard C, Pascot A, Cantin B, Bergeron J, et al. Total cholesterol/HDL cholesterol ratio vs LDL cholesterol/HDL cholesterol ratio as indices of ischemic heart disease risk in men: the Quebec Cardiovascular Study. Arch Intern Med. 2001;161:2685–92.
16. National Statistical Office of Korea. Population and Housing Census Statistical Survey. 2005. http://www.kosis.nso.go.kr. Accessed 15 Dec 2009.
17. Kinosian B, Glick H, Garland G. Cholesterol and coronary heart disease: predicting risks by levels and ratios. Ann Intern Med. 1994;121:641–7.
18. Stampfer MJ, Sacks FM, Salvini S, Willett WC, Hennekens CH. A prospective study of cholesterol, apolipoproteins, and the risk of myocardial infarction. N Engl J Med. 1991;325:373–81.
19. Ingelsson E, Schaefer EJ, Contois JH, McNamara JR, Sullivan L, Keyes MJ, et al. Clinical utility of different lipid measures for prediction of coronary heart disease in men and women. JAMA. 2007;298:776–85.

20. Lee S, Choi S, Kim HJ, Chung YS, Lee KW, Lee HC, et al. Cutoff values of surrogate measures of insulin resistance for metabolic syndrome in Korean non-diabetic adults. J Korean Med Sci. 2006;21:695–700.
21. Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of the National Cholesterol Education Program (NCEP) Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001;285:2486–97.
22. Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diab Res Clin Pract. 2007;75:72–80.
23. Gabir MM, Hanson RL, Dabelea D, Imperatore G, Roumain J, Bennett PH, et al. The 1997 American Diabetes Association and 1999 World Health Organization criteria forhyperglycemia in the diagnosis and prediction of diabetes. Diab Care. 2000;23:1108–12.
24. Shaw JE, Zimmet PZ, Hodge AM, de Courten M, Dowse GK, Chitson P, et al. Impaired fasting glucose: how low should it go? Diab Care. 2000;23:34–9.
25. Hanna-Moussa A, Gardner MJ, Kurukulasuriya LR, Sowers JR. Dysglycemia/prediabetes and cardiovascular risk factors. Rev Cardiovasc Med. 2009;10:202–8.
26. Rhee EJ, Kim YC, Lee WY, Jung CH, Sung KC, Ryu SH, et al. Comparison of insulin resistance and semm high-sensitivity C-reactive protein levels according to the fasting blood glucose subgroups divided by the newly recommended criteria for fasting hyperglycemia in 10059 healthy Koreans. Metab Clin Exp. 2006;55:183–7.
27. Chang SA, Kim HS, Yoon KH, Ko SH, Kwon HS, Kim SR, et al. Body mass index is the most important determining factor for the degree of insulin resistance in non-obese type 2 diabetic patients in Korea. Metabolism. 2004;53:142–6.