1-Hour and 2-Hour Postload Glucose Level on Oral Glucose Tolerance Test and the Risk of Incident Metabolic Syndrome

Sung Keun Park,[1] Jae-Hong Ryoo,[2] Chang-Mo Oh,[3] Joong-Myung Choi,[3] and Ju Young Jung[4]

[1]Center for Cohort Studies, Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul 110-746, Korea; [2]Department of Occupational and Environmental Medicine, College of Medicine, Kyung Hee University, Seoul 02447, Korea; [3]Departments of Preventive Medicine, School of Medicine, Kyung Hee University, Seoul 02447, Korea; and [4]Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, Seoul 110-746, Korea

ORCiD numbers: 0000-0001-7921-6549 (J. Y. Jung).

Background: Metabolic syndrome (MetS) increases the cardiometabolic risk even in nondiabetic patients. Previous studies have demonstrated that 1-hour postload glucose (PG) and 2-hour PG based on oral glucose tolerance test (OGTT) predicted cardiometabolic risk. However, it is still unclear whether and to what extent postload glucose is associated with the risk of MetS.

Methods: A total of 5389 nondiabetic Koreans were dichotomized into normoglycemic (NG) groups and abnormal glycemic groups based on OGTT, including elevated 1-hour PG (155 to 199 mg/dL) and impaired glucose tolerance (IGT) (2-hour PG 140 to 199 mg/dL), and followed up for 10 years. Cox proportional hazard model was used to evaluate hazard ratios (HRs) with 95% CIs for incident MetS. Subgroups were determined by high or normal 1-hour PG (cutoff: 155 mg/dL) and 2-hour PG (cutoff: 140 mg/dL).

Results: Compared with NG, the risk of MetS increased proportionally to the level of 1-hour PG and 2-hour PG, independently of the number of baseline metabolic components. Even within people with normoglycemia, elevated PG above specific levels (1-hour PG ≥115 mg/dL and 2-hour PG ≥100 mg/dL) was significantly associated with the increased risk of MetS. In subgroup analysis, adjusted HR for MetS was higher in the group with high 1-hour PG and normal 2-hour PG [1.53 (95% CI, 1.35 to 1.74)] than in the group with normal 1-hour PG and high 2-hour PG [1.32 (95% CI, 1.02 to 1.70)].

Conclusion: Elevated 1-hour PG and 2-hour PG significantly are associated with greater risk for MetS, and 1-hour PG was superior to 2-hour PG in predicting MetS. (***J Clin Endocrinol Metab*** **104: 539–549, 2019)**

Metabolic syndrome (MetS) is a cluster of at least three of five medical conditions: abdominal obesity, high blood pressure (BP), high blood glucose, high triglyceride, and low high-density lipoprotein-cholesterol (HDL-C) (1). Transition to a sedentary lifestyle, decrease in physical activity, and high calorie intake with animal

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in USA

Received 21 May 2018. Accepted 13 September 2018.
First Published Online 18 September 2018

Abbreviations: AUC_{ROC}, area under the receiver operating characteristic curve; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; H1H2, high 1-hour postload glucose and high 2-hour postload glucose; H1N2, high 1-hour postload glucose and normal 2-hour postload glucose; HDL-C, high-density lipoprotein-cholesterol; HR, hazard ratio; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; IR, insulin resistance; KoGES, Korean Genome and Epidemiology Study; MetS, metabolic syndrome; N1H2, normal 1-hour postload glucose and high 2-hour postload glucose; N1N2, normal 1-hour postload glucose and normal 2-hour postload glucose; NG, normoglycemic; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; PG, postload glucose; ROC, receiver operating characteristic; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus.

fat have contributed to the increased global prevalence of MetS. Approximately 20% to 25% of adults worldwide are presumed to have MetS (2), and this trend is remarkable in East Asia with its rapid economic growth. In the Korean National Health and Nutrition Examination Survey, the age-adjusted prevalence of MetS was 24.9% in 1998 and 31.3% in 2007, with an estimated 0.6% annual increase over 10 years (3). A meta-analysis of published studies in China indicated that the prevalence of MetS was growing particularly among women, urbanites, and older adults, with a nationwide prevalence of 24.5% (4).

MetS is a strong risk factor for cardiometabolic diseases such as type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD), imposing substantial health care costs. Given that Asians are more predisposed to cardiometabolic disease than Caucasians at the same degree of obesity (5–7), the growing prevalence of MetS may impose a more serious burden on public health in Asia. Thus, it is worth identifying the risk factors of MetS in terms of preventing the adverse health outcomes related to MetS.

Insulin resistance (IR) plays a pivotal role in the pathophysiology of MetS as an underlying mechanism (8). Impaired fasting glucose (IFG) is both a clinical sign of IR and a component of MetS, and abdominal obesity is related to visceral adiposity, aggravating IR. Additionally, several studies have reported that IR is closely linked to elevated BP and dyslipidemia. Thus, it is postulated that categories of abnormal glucose homeostasis reflecting IR are effective in assessing the risk of incident MetS.

Both fasting glucose measurements and oral glucose tolerance tests (OGTTs) are commonly used to identify abnormal glucose homeostasis. Previous studies have demonstrated that postchallenge hyperglycemia, measured as a continuous variable, is a better predictor of coronary heart disease than fasting hyperglycemia (9, 10). Additionally, impaired glucose tolerance (IGT) based on OGTT was associated with more factors included in MetS (11) and an increased risk for CVD (9, 12). In particular, the Baltimore Longitudinal Study indicated that the people with IGT had a higher prevalence of MetS compared with people with IFG (13), despite the fact that IFG is a component of MetS. These results suggest that OGTT is useful for identifying people with the increased risk of MetS. Although 2-hour postload glucose (PG) is a basic indicator in interpreting OGTT (14), 1-hour PG as measured by OGTT has been increasingly recognized as important in predicting cardiometabolic risk. In recent cohort studies, 1-hour PG was a better predictor of the development of T2DM than 2-hour PG (15–17), representing the higher correlation with decreased insulin secretion and action as indicated by insulinogenic index and disposition index (15, 16). In particular, accumulated evidence has highlighted the clinical significance of a cutoff of 1-hour PG of 155 mg/dL, which was effective in distinguishing patients with elevated cardiovascular risk from those with normal glucose tolerance (NGT) (18). These results led to a hypothesis that elevated 1-hour PG is connected to the increased risk of incident MetS, associated with the components of MetS. However, the relationship between 1-hour PG and incident MetS has been less well described.

Using data from the Korean Genome and Epidemiology Study (KoGES), we evaluated the risk of incident MetS according to the levels of 1-hour PG and 2-hour PG based on OGTT. To compare the predictive ability of 1-hour PG and 2-hour PG for MetS, we conducted subgroup analyses defined by each category of 1-hour PG and 2-hour PG.

Research Design and Methods

Study population

All subjects were participants in the KoGES Ansan and Ansung Study, which is a population-based epidemiological study of rural and urban communities in South Korea. Detailed methods and the study population of the current study are described in the previous study (19). The baseline survey of the KoGES Ansan and Ansung study was completed in 2001 to 2002, and follow-up surveys were conducted every 2 years. Initially, a total of 10,038 participants aged 40 to 69 participated in the study. A total of 5018 participants were recruited by cluster-sampling method, stratified by age, sex, and residential district in the Ansung community, and 5020 subjects were selected by random sampling method in Ansan. Of these 10,038 participants, we eliminated 829 subjects who had missing data for history of diabetes, HbA1c, fasting 1-hour PG, and 2-hour PG. Among 9209 participants, 3211 participants with baseline MetS (n = 2840), diabetes mellitus (DM), or IFG (n = 371) were excluded. Thus, the number of subjects who initially enrolled in follow-up was 5998.

Over 10 years of follow-up, 609 additional subjects were excluded because of attrition or incomplete follow-up data. Finally, the total number of study participants was 5389 (Fig. 1). All subjects participated in the study voluntarily, and informed consent was obtained in all cases. Ethics approvals for the study protocol and analysis of the data were obtained from the institutional review board of Kangbuk Samsung Hospital.

Clinical and biochemical measurements

Study data included a medical history and sociodemographic information provided by a self-administered questionnaire, anthropometric measurements, and laboratory biochemical measurements. All study participants were also asked to respond to a health-related behavior questionnaire, which included the topics of alcohol consumption, smoking, and exercise. Physical activity was divided two categories: regular exercise (≥90 minutes exercise per week, at least moderate

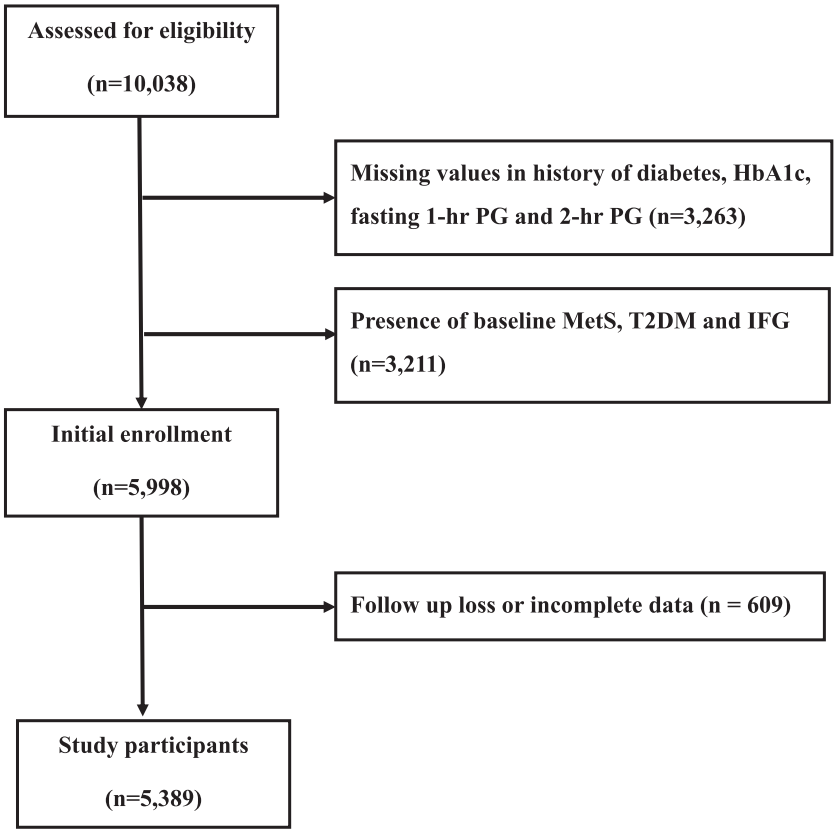

Figure 1. Flowchart of enrolled study participants.

intensity) or inactive. The questions about alcohol intake included the frequency of alcohol consumption on a weekly basis and the typical amount that was consumed on a daily basis (in grams per day). Smoking status was divided into three categories: never, former, and current smoker. DM was defined as fasting serum glucose ≥126 mg/dL, serum HbA1c ≥6.5%, 2-hour PG ≥200 mg/dL, or history of diagnosed DM (14). Hypertension was determined in the participants with a diagnosis of hypertension or with a measured systolic blood pressure (SBP) ≥140 or diastolic blood pressure (DBP) ≥90 mm Hg at initial examination. BP was measured in both arms in the sitting position after participants had been in a relaxed state for ≥10 minutes. There was a 5-minute rest period between measurements. The arithmetic mean value of the BP was used to define the SBP and DBP. All participants' waist circumference, height, and weight were also measured, and body mass index (BMI) was calculated.

After participants fasted overnight for 12 hours, the plasma concentrations of glucose, total cholesterol, triglyceride, and HDL-C were measured enzymatically with a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). In the baseline and follow-up examinations, all study participants underwent OGTT, which was interpreted by 1-hour PG and 2-hour PG. Conventional cutoffs of 1-hour PG (155 mg/dL) and 2-hour PG (140 mg/dL) were used in identifying abnormal glycemic states (1, 20), and a PG level lower than cutoff was regarded as normoglycemia.

Fasting plasma insulin concentrations were determined by a radioimmunoassay kit (Linco Research, St. Charles, MO). The HbA1c level was measured by high-performance liquid chromatography (VARIANT II; Bio-Rad Laboratories, Hercules, CA).

MetS was diagnosed according to the definition of the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention (1). Elevated BP was defined as SBP ≥130 mm Hg or DBP ≥85 mm Hg; elevated fasting serum glucose level was defined as ≥100 mg/dL; high serum triglyceride levels were defined as ≥150 mg/dL; low HDL-C levels were defined as <40 mg/dL in men and <50 mg in women. The presence of abdominal obesity was defined according to the criteria of the Korean Society of the Study of Obesity (waist circumference ≥90 cm for men and ≥85 cm for women) (21). The presence of MetS was defined as the presence of three or more of the aforementioned components.

Statistical analysis

Study participants were categorized into one of two groups by the cutoffs for 1-hour PG and 2-hour PG. Data are presented as means ± SD within study groups for continuous variables and as proportions for categorical variables. Main clinical characteristics and biochemical parameters between the two groups were compared by independent *t* test for continuous variables and χ^2 test for categorical variables.

The crude and multivariate-adjusted hazard ratios (HRs) and their 95% CI for MetS were estimated with the use of the Cox proportional hazards model [adjusted HRs (95% CI)]. Covariates of the adjusted model were age, sex, area, regular exercise, BMI, hypertension, smoking, alcohol intake, and HDL-C. The incidence cases of MetS and incidence density (incidence cases per 1000 person-years) were calculated for each study group.

To analyze the risk of MetS according to PG levels, participants with abnormal glycemic states were subdivided into three groups by level of 1 hour-PG (155 to 174 mg/dL, 175 to 194 mg/dL, and ≥195 mg/dL) and 2-hour PG (140 to 159 mg/dL, 160 to 179 mg/dL, and 180 to 199 mg/dL), and participants with normal glycemic states were subdivided into four groups by level of 1 hour-PG (<95 mg/dL, 95 to 114 mg/dL, 115 to 134 mg/dL, and 135 to 154 mg/dL) and 2-hour PG (<80 mg/dL, 80 to 99 mg/dL, 100 to 119 mg/dL, and 120 to 139 mg/dL).

The number of baseline metabolic components (0 to 1 and 2) was used to set two upper categories in analysis. In each category (number of baseline metabolic components: 0 to 1 and 2), adjusted HRs for MetS and 95% CI were estimated according to levels of elevated 1-hour PG and 2-hour PG.

In the subgroup analysis comparing the predictive ability of 1-hour PG and 2-hour PG, four subgroups were defined by high or normal 1-hour PG and 2-hour PG, determined by conventional cutoffs (155 mg/dL for 1-hour PG and 140 mg/dL for 2-hour PG) as follows: normal 1-hour PG (<155 mg/dL) and normal 2-hour PG (<140 mg/dL) (N1N2), high 1-hour PG (≥155 mg/dL) and normal 2-hour PG (<140 mg/dL) (H1N2), normal 1-hour PG (<155 mg/dL) and high 2-hour PG (≥140 mg/dL) (N1H2), and high 1-hour PG (≥155 mg/dL) and high 2-hour PG (≥140 mg/dL) (H1H2). The trend analysis was calculated based on the median value of each group.

To verify the reliability of the analyzed data, we separated our study participants into a discovery sample and a validation sample. Through random sampling, 70% of study participants were classified as discovery samples and the remaining 30% were classified as validation samples. The area under the receiver operating characteristic curve (AUC_{ROC}) of 1-hour PG and 2-hour PG for MetS were assessed in both the discovery sample and the validation sample. DeLong's test was used in comparing the AUC_{ROC} between 1-hour PG and 2-hour PG.

In the discovery sample, we calculated the potential cutoffs of 1-hour PG and 2-hour PG for MetS and their specificity and sensitivity by bootstrapping (1000 stratified bootstrap replicates in each analysis). Cutoff points were determined to maximize the Youden index on the receiver operating characteristic (ROC) curve using the "pROC" package. The calculated cutoff in discovery sample was applied to the validation sample, in which the specificity and sensitivity of the applied cutoff was evaluated.

Using the cutoffs of 1-hour PG and 2-hour PG calculated for the discovery group, we conducted an analysis for four subgroups with N1N2, H1N2, N1H2, and H1H2 for all study participants.

All statistical analyses were performed with R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria), and $P < 0.05$ was considered statistically significant in all analyses.

Results

A total of 5389 participants were enrolled in the study (2633 men and 2756 women). The overall incidence of MetS was 28.6% (n = 1540), and the mean age of study participants was 50.6 ± 8.6 years. The final follow-up examination was done in 2011 or 2012. The baseline clinical and biochemical characteristics of study participants are presented in Table 1. The groups with abnormal glucose tolerance (1-hour PG ≥155 mg/dL and 2-hour PG ≥140 mg/dL) tended to have worse cardiometabolic profiles, including incidence of MetS, age, 1-hour PG, 2-hour PG, HbA1c, fasting glucose, total cholesterol, and triglyceride than the NGT groups.

Table 2 represents the unadjusted and adjusted HRs and 95% CIs for MetS for each 1-hour PG and 2-hour PG group. When normoglycemic (NG) states (1-hour PG <155 mg/dL and 2-hour PG <140 mg/dL) were set as references, the adjusted HRs for MetS significantly increased proportionally to the levels of 1-hour PG and 2-hour PG. In the analysis for 2-hour PG, the highest level of 2-hour PG had an adjusted HR more than two times higher than that of the lowest level of 2-hour PG (140 to 159 mg/dL: 1.36, 95% CI, 1.16 to 1.60; 160 to 179 mg/dL: 1.81, 95% CI, 1.47 to 2.25; 180 to 199 mg/dL: 2.21, 95% CI, 1.66 to 2.95), which was statistically significant ($P < 0.001$). Analysis for 1-hour PG also showed the identical pattern (155 to 174 mg/dL: 1.45, 95% CI, 1.26 to 1.67; 175 to 194 mg/dL: 1.82, 95% 1.56 to 2.13; ≥195 mg/dL: 1.83, 95% CI, 1.54 to 2.18).

Even for participants in an NG state, both 1-hour PG and 2-hour PG above specific levels were significantly associated with increased risk for MetS (Table 3). Adjusted HRs for MetS increased proportionally to level of

Table 1. Baseline Clinical Characteristics According to 1-h and 2-h Plasma Glucose Levels

	2-H Plasma Glucose			1-H Plasma Glucose		
Characteristics	**<140 mg/dL (N = 4483)**	**≥140 mg/dL (N = 906)**	***P***	**<155 mg/dL (N = 3693)**	**≥155 mg/dL (N = 1696)**	***P***
Male sex, n (%)	2243 (50.0%)	390 (43.0%)	<0.001	1706 (46.2%)	927 (54.7%)	<0.001
Age, y	50.4 ± 8.5	52.5 ± 8.9	<0.001	49.8 ± 8.3	52.6 ± 9.0	<0.001
Fasting glucose, mg/dL	81.1 ± 7.0	83.8 ± 7.7	<0.001	80.3 ± 6.8	84.3 ± 7.4	<0.001
1-h PG, mg/dL	129.4 ± 35.7	173.6 ± 33.7	<0.001	115.8 ± 23.9	182.6 ± 23.4	<0.001
2-h PG, mg/dL	101.3 ± 20.8	158.7 ± 15.5	<0.001	102.3 ± 23.3	129.8 ± 32.1	<0.001
Fasting insulin, μIU/mL	7.0 ± 4.3	7.0 ± 3.8	0.535	7.1 ± 4.4	6.8 ± 3.8	0.006
HbA1c, %	5.5 ± 0.3	5.6 ± 0.3	<0.001	5.4 ± 0.3	5.6 ± 0.3	<0.001
Total cholesterol, mg/dL	186.1 ± 33.4	194.3 ± 36.7	<0.001	185.2 ± 33.3	192.5 ± 35.4	<0.001
Triglyceride, mg/dL	130.3 ± 76.2	142.2 ± 85.8	<0.001	130.2 ± 74.4	139.0 ± 88.9	<0.001
HDL-C, mg/dL	46.8 ± 9.9	47.5 ± 10.7	0.058	46.3 ± 9.8	48.1 ± 10.5	0.058
Height, cm	160.6 ± 8.5	159.1 ± 8.2	<0.001	160.3 ± 8.5	160.4 ± 8.4	0.766
Weight, kg	61.2 ± 9.3	60.8 ± 9.5	0.241	61.0 ± 9.3	61.3 ± 9.4	0.283
BMI, kg/m^2	23.7 ± 2.8	24.0 ± 3.1	0.004	23.7 ± 2.7	23.8 ± 3.0	0.004
Waist circumference, cm	79.5 ± 7.6	79.5 ± 7.8	0.984	79.3 ± 7.6	80.2 ± 7.8	<0.001
SBP, mm Hg	115.8 ± 16.1	118.6 ± 18.0	<0.001	114.7 ± 16.0	119.7 ± 17.0	<0.001
DBP, mm Hg	77.3 ± 10.6	78.1 ± 11.0	<0.001	76.5 ± 10.4	79.3 ± 11.0	<0.001
Average alcohol use, g/d	8.9 ± 20.5	8.9 ± 22.3	1.000	8.0 ± 19.8	11.0 ± 22.8	<0.001
Current smoking, %	24.2%	18.8%	0.001	22.2%	25.8%	<0.001
Regular exercise, %	41.2%	31.0%	<0.001	39.8%	38.9%	0.540
Hypertension, %	17.4%	23.7%	<0.001	15.1%	25.8%	<0.001
Incidence of MetS, n (%)	1226 (27.3%)	314 (34.7%)	<0.001	922 (25.0%)	618 (36.4%)	<0.001

Continuous variables are expressed as mean (±SD), and categorical variables are expressed as number (%).

Table 2. HRs and 95% CIs for Incident MetS According to 1-h PG and 2-h PG Levels

Characteristics	Unadjusted HR	Adjusted HR	Incidence Cases	Incidence Density
1-h PG				
<155 mg/dL (n = 3693)	Reference (1.00)	Reference (1.00)	992	33.0
155–174 mg/dL (n = 769)	1.49 (1.30–1.70)	1.45 (1.26–1.67)	264	47.7
175–194 mg/dL (n = 500)	1.84 (1.58–2.15)	1.82 (1.56–2.13)	201	58.2
≥195 mg/dL (n = 427)	1.73 (1.46–2.06)	1.83 (1.54–2.18)	153	53.8
P for trend	<0.001	<0.001		
2-h PG				
<140 mg/dL (n = 4483)	Reference (1.00)	Reference (1.00)	1226	36.6
140–159 mg/dL (n = 535)	1.26 (1.07–1.48)	1.36 (1.16–1.60)	172	45.3
160–179 mg/dL (n = 245)	1.53 (1.24–1.89)	1.81 (1.47–2.25)	93	53.6
180–199 mg/dL (n = 126)	1.82 (1.37–2.42)	2.21 (1.66–2.95)	49	61.9
P for trend	<0.001	<0.001		

Adjusted for age, sex, study area (Ansan or Ansung), hypertension, regular exercise, BMI, smoking, HDL-C, and alcohol intake. Incidence density is measured as incidence cases per 1000 person-years.

1-hour PG from 115 mg/dL to 154 mg/dL (115 to 134 mg/dL: 1.26, 95% CI, 1.03 to 1.54; 135 to 154 mg/dL: 1.49, 95% CI, 1.22 to 1.83). This association was reproduced in 2-hour PG with NG states (100 to 119 mg/dL: 1.22, 95% CI, 1.01 to 1.47; 120 to 139 mg/dL: 1.39, 95% CI, 1.14 to 1.70).

The subgroup analysis according to the number of baseline metabolic components is presented in Table 4. In the groups with baseline metabolic components of 0 to 1, adjusted HRs for MetS proportionally increased from 1-hour PG >155 mg/dL and 2-hour PG >160 mg/dL. Subgroups with baseline metabolic components of 2 showed that adjusted HRs for MetS proportionally increased above the cutoffs for 1-hour PG and 2-hour PG.

In an analysis for four subgroups determined by high or normal 1-hour PG and 2-hour PG, compared with the N1N2 group, the H1H2 group had the highest adjusted HRs for MetS (1.93; 95% CI, 1.67 to 2.22) (Table 5). The H1N2 group had higher adjusted HRs for MetS (1.53; 95% CI, 1.35 to 1.74) than the N1H2 group (1.32; 95% CI, 1.02 to 1.70). Table 5 also presents the analysis for four subgroups determined by cutoffs calculated in the discovery sample (142.5 mg/dL 1-hour PG and 107.5 mg/dL 2-hour PG). Similarly to the results from the subgroup analysis with conventional cutoffs, the H1N2 group had higher adjusted HRs for MetS (1.47; 95% CI, 1.24 to 1.73) than the N1H2 group (1.13; 95% CI, 0.97 to 1.31).

Table 6 shows the AUC_{ROC} and 95% CI for 1-hour PG and 2-hour PG for Met S analyzed in the discovery and validation samples. In the discovery sample, AUC_{ROC} for 1-hour PG (0.576; 95% CI, 0.545 to 0.608) was significantly higher than that of the 2-hour PG (0.525; 95% CI, 0.493 to 0.557) ($P < 0.001$). Analyzed optimal cutoffs were 142.5 mg/dL for 1-hour PG and 107.5 mg/dL for 2-hour PG, with specificity/sensitivity of 62.7%/51.9% and 51.6%/56.3%, respectively. These findings were similarly observed in the validation sample. AUC_{ROC} for the validation sample was 0.576 (95% CI,

Table 3. HRs and 95% CIs for Incident MetS According to 1-h PG and 2-h PG Levels for NG Participants

Characteristics	Unadjusted HR	Adjusted HR	Incidence Density	Incidence Cases
1-h PG				
<95 mg/dL (n = 752)	Reference (1.00)	Reference (1.00)	26.2	153
95–114 mg/dL (n = 936)	1.15 (0.93–1.41)	1.10 (0.89–1.35)	29.9	217
115–134 mg/dL (n= 1050)	1.34 (1.10–1.63)	1.26 (1.03–1.54)	34.9	278
135–154 mg/dL (n = 955)	1.58 (1.29–1.92)	1.49 (1.22–1.83)	39.8	274
P for trend	<0.001	<0.001		
2-h PG				
<80 mg/dL (n = 671)	Reference (1.00)	Reference (1.00)	31.3	159
80–99 mg/dL (n = 1338)	1.12 (0.92–1.35)	1.13 (0.94–1.37)	34.7	350
100–119 mg/dL (n = 1504)	1.20 (1.00–1.45)	1.22 (1.01–1.47)	37.0	417
120–139 mg/dL (n = 970)	1.41 (1.16–1.71)	1.39 (1.14–1.70)	42.6	300
P for trend	<0.001	<0.001		

Adjusted for age, sex, study area (Ansan or Ansung), hypertension, regular exercise, BMI, smoking, HDL-C, and alcohol intake. Incidence density is measured as incidence cases per 1000 person-years.

Table 4. HRs and 95% CIs for Incident MetS According to 1-h PG and 2-h PG Levels in Each Category Stratified by the Number of Baseline Metabolic Components

Characteristics	Unadjusted HR	Adjusted HR	Incidence Density	Incidence Cases
0 or 1 metabolic component				
1-h PG				
<155 mg/dL (n = 2246)	Reference (1.00)	Reference (1.00)	20.9	404
155–174 mg/dL (n = 482)	1.54 (1.25–1.89)	1.49 (1.20–1.83)	31.1	114
175–194 mg/dL (n = 303)	1.92 (1.52–2.42)	2.00 (1.58–2.53)	38.8	88
≥195 mg/dL (n = 266)	1.43 (1.08–1.89)	1.59 (1.19–2.12)	28.5	56
P for trend	<0.001	<0.001		
2-h PG				
<140 mg/dL (n = 2954)	Reference (1.00)	Reference (1.00)	23.3	539
140–159 mg/dL (n = 316)	1.19 (0.92–1.54)	1.28 (0.99–1.66)	27.4	66
160–179 mg/dL (n = 148)	1.34 (0.95–1.89)	1.43 (1.01–2.02)	30.6	35
180–199 mg/dL (n = 79)	1.79 (1.17–2.74)	2.28 (1.47–3.52)	39.5	22
P	0.002	<0.001		
2 metabolic components				
1-h PG				
<155 mg/dL (n = 1247)	Reference (1.00)	Reference (1.00)	60.0	518
155–174 mg/dL (n = 287)	1.37 (1.14–1.64)	1.39 (1.15–1.69)	80.5	150
175–194 mg/dL (n = 197)	1.70 (1.38–2.08)	1.69 (1.37–2.08)	95.3	113
≥195 mg/dL (n = 161)	2.05 (1.65–2.55)	2.04 (1.63–2.54)	110.2	97
P for trend	<0.001	<0.001		
2-h PG				
<140 mg/dL (n = 1529)	Reference (1.00)	Reference (1.00)	66.3	687
140–159 mg/dL (n = 219)	1.17 (0.95–1.43)	1.39 (1.13–1.72)	76.3	106
160–179 mg/dL (n = 97)	1.62 (1.24–2.12)	2.16 (1.64–2.84)	99.9	58
180–199 mg/dL (n = 47)	2.01 (1.39–2.95)	2.24 (1.52–3.31)	115.1	27
P for trend	<0.001	<0.001		

Adjusted for age, sex, study area (Ansan or Ansung), hypertension, regular exercise, BMI, smoking, HDL-C, and alcohol intake. Incidence density is measured as incidence cases per 1000 person-years.

0.545 to 0.608) for 1-hour PG and 0.525 (95% CI, 0.493 to 0.557) for 2-hour PG. Specificity/sensitivity of optimal cutoff was 61.3%/50.3% for 1-hour PG and 49.8%/55.5% for 2-hour PG. The aforementioned AUC_{ROC}, optimal cutoffs of 1-hour and 2-hour PG, and their specificity/sensitivity for MetS are schematically presented in Figs. 2 and 3.

Discussion

MetS is an aggregation of cardiometabolic risks including abdominal obesity, IR, dyslipidemia, and hypertension, which profoundly contributes to the development of T2DM, CVD, and related mortality. Thus, early recognition and proper management of the risk factors for

Table 5. HRs and 95% CIs for Incident MetS According to 4 Subgroups Determined by High or Normal 1-h PG and 2-h PG

Characteristics	Unadjusted HR	Adjusted HR	Incidence Density	Incidence Cases
Conventional cutoff point				
N1N2 (n = 3453)	Reference (1.00)	Reference (1.00)	32.8	859
N1H2 (n =240)	1.12 (0.86–1.44)	1.32 (1.02–1.70)	35.9	63
H1N2 (n= 1030)	1.60 (1.41–1.81)	1.53 (1.35–1.74)	50.5	367
H1H2 (n = 666)	1.76 (1.53–2.02)	1.93 (1.67–2.22)	55.0	251
P for trend	<0.001	<0.001		
Optimal cutoff point, mg/dL				
N1N2 (n = 2046)	Reference (1.00)	Reference (1.00)	30.2	475
N1H2 (n = 1097)	1.11 (0.95–1.28)	1.13 (0.97–1.31)	32.7	272
H1N2 (n = 597)	1.62 (1.37–1.91)	1.47 (1.24–1.73)	47.3	202
H1H2 (n = 1649)	1.79 (1.59–2.02)	1.78 (1.57–2.02)	51.5	591
P for trend	<0.001	<0.001		

Adjusted for age, sex, study area (Ansan or Ansung), hypertension, regular exercise, BMI, smoking, HDL-C, and alcohol intake. Incidence density is measured as incidence cases per 1000 person-years. Conventional cutoff point: 155 mg/dL for 1-h PG, 140 mg/dL for 2-h PG. Optimal cutoff point: 142.5 mg/dL for 1-h PG, 107.5 mg/dL for 2-h PG.

Table 6. AUC and Optimal Cutoff Points of ROC Curve for Discovery and Validation Samples of Study Population

Characteristics	AUC_{ROC} (95% CI)	Optimal Cutoff Point, mg/dL	Specificity/ Sensitivity	*P*[a]
Discovery sample (n = 3772)				
1-h PG	0.587 (0.568–0.607)	142.5	62.7%/51.9%	<0.001
2-h PG	0.562 (0.542–0.582)	107.5	51.6%/56.3%	
Validation sample (n = 1617)				
1-h PG	0.576 (0.545–0.608)	142.5	61.3%/50.3%	<0.001
2-h PG	0.525 (0.493–0.557)	107.5	49.8%/55.5%	

[a]DeLong tests were used to compare AUCs of two correlated ROC curves.

MetS are important for preventing MetS and maintaining health.

In the MetS-free general Korean population without T2DM and IFG, we assessed the predictive ability of 1-hour PG and 2-hour PG based on OGTT for the development of MetS. Our results presented the several interesting findings regarding the association between PG on OGTT and MetS.

The first major finding is that the risk of MetS was significantly higher in participants with abnormal glycemia, defined by 1-hour PG or 2-hour PG based on OGTT. A 1-hour PG ≥155 mg/dL was significantly associated with increased risk of MetS, which was also observed for 2-hour PG ≥140 mg/dL. Previous studies have also suggested a close link between MetS and PG levels on OGTT. Despite the scarce results directly

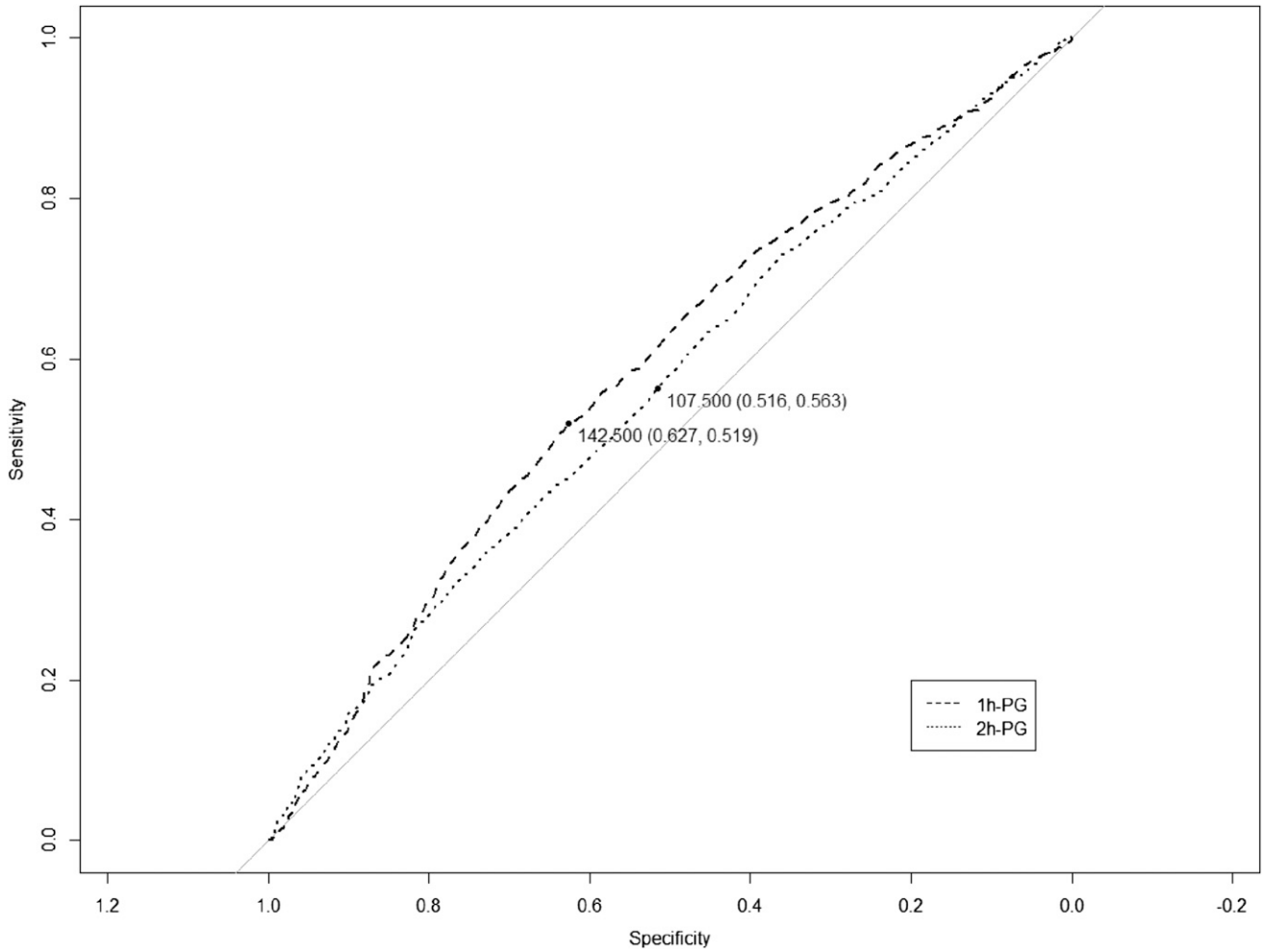

Figure 2. AUC_{ROC} for 1-h PG (cutoff, 142.5 mg/dL; specificity/sensitivity, 62.7%/51.9%) and 2-h PG (cutoff, 107.5 mg/dL; specificity/sensitivity, 51.6%/56.3%) in the discovery sample.

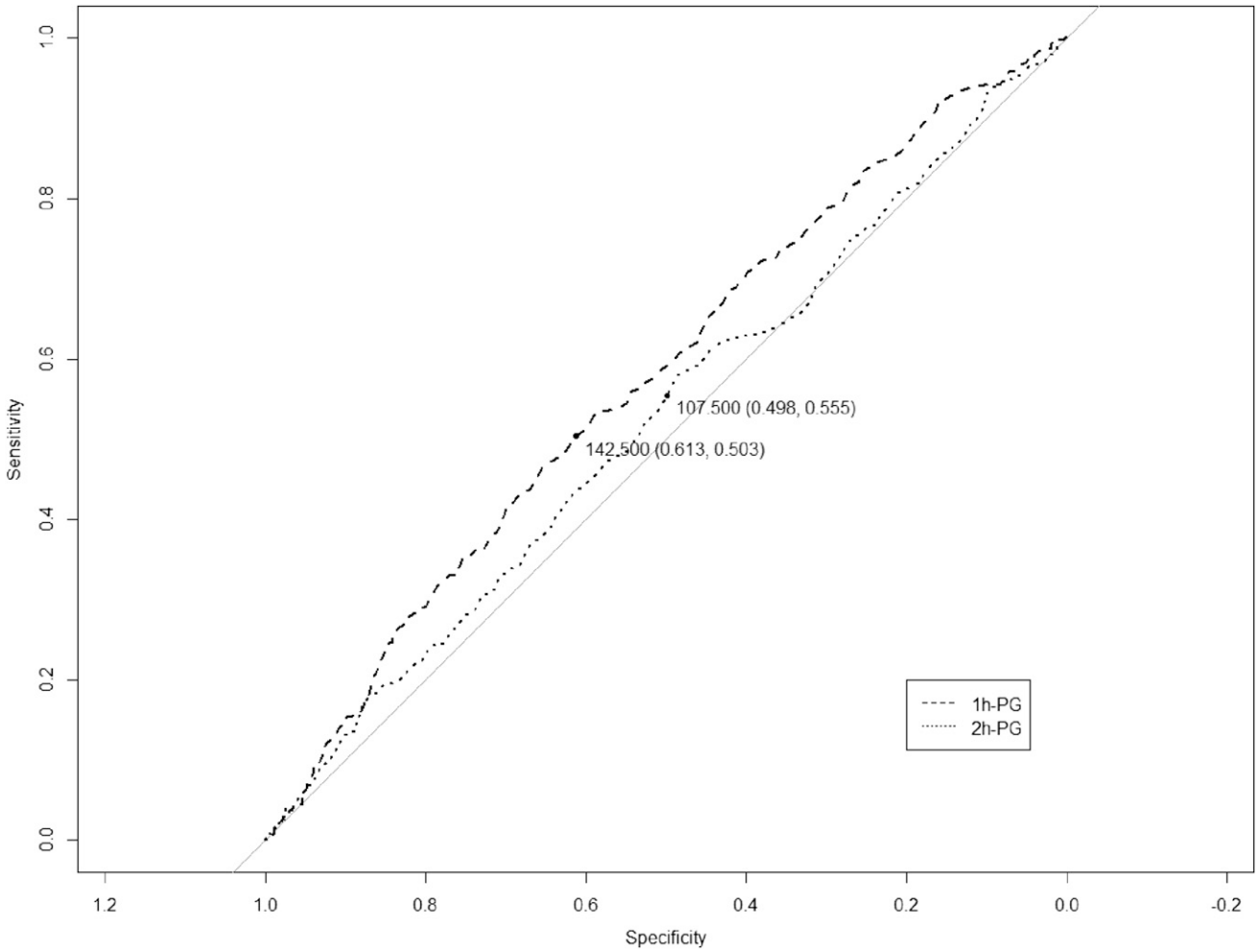

Figure 3. AUC_{ROC} for 1-h PG (cutoff, 142.5 mg/dL; specificity/sensitivity, 61.3%/50.3%) and 2-h PG (cutoff, 107.5 mg/dL; specificity/sensitivity, 49.8%/55.5%) in the validation sample.

indicating the influence of IGT on MetS, cross-sectional studies for multiethnic participants demonstrated a significant association between IGT and MetS. In 928 Chinese adults, MetS was associated with about a threefold increase in the risk of IGT, effectively distinguishing subjects with IGT from those with NGT, and the clustering of any one, two, or three or more metabolic components resulted in proportionally increased ORs (1.71, 2.38, and 5.92) for IGT (22). These findings were similarly observed in a study of white Americans, Mexican Americans, and African Americans that MetS was linked to IGT, with ORs of 3 to 4 (23). In particular, it is of note that 1-hour PG was related to the long-term risk of MetS in our study. In current guideline, patients with a 1-hour PG of 155 to 199 mg/dL and 2-hour PG <140 mg/dL were classified into NGT (NGT 1-hour high) despite the elevated 1-hour PG above cutoff (14). The diagnostic value of 1-hour PG has been increasingly recognized in such patients with NGT 1-hour high. Several studies have reported that NGT 1-hour high was characterized by metabolic abnormality similar to that in IGT (24, 25). In a study of Chinese patients with coronary heart disease, group with 1-hour PG ≥155 mg/dL had the higher BMI, SBP, and triglycerides and lower HDL-C (24). Additionally, a study of 94 overweight or obese patients showed that 1-hour PG correlates well with fasting glucose and 2-hour PG, representing similar or greater associations with obesity, hypertension, hypercholesterolemia, and MetS (25). However, there was only limited information about the longitudinally investigated relationship between elevated 1-hour PG and incident MetS. In a 10-year retrospective cohort study of 116 Chinese patients, the prevalence of MetS was 34.6% in subjects with elevated baseline 1-hour PG ≥160 mg/dL and 18.9% in subjects with baseline 1-hour PG <160 mg/dL (26). However, their sample size was too small to show the statistical significance of the difference in prevalence of MetS and values of metabolic components. In contrast, our results clearly indicate that elevated 1-hour PG ≥155 mg/dL increases the risk of MetS. Given that MetS is implicated in the

development of cardiometabolic disease, patients with elevated 1-hour PG may need close monitoring and proper management for MetS, regardless of 2-hour PG.

On OGTT, there is the wide range of PGs defining the specific categories of glycemic states such as NGT and IGT. The nondiabetic range of 1-hour PG above cutoff is 155 to 199 mg/dL, and IGT is defined as a 2-hour PG of 140 to 199 mg/dL. Thus, it is inferred that patients even in same glycemic state can differ in cardiometabolic risk according to their PG levels. When we assessed the risk for MetS according to the stratified 1-hour PG and 2-hour PG levels above each conventional cutoff, we found a stepwise increase in the risk for MetS proportionate to each PG level. Moreover, even within the NG groups, the risk for MetS proportionally increased from the specific 1-hour PG and 2-hour PG levels. These findings verify our hypothesis that patients with higher PG have a higher risk for MetS within a same glycemic state category. Thus, it is postulated that the selective approach is necessary to stratify the risk of MetS even within patients with same glycemic state. A 1-hour PG and 2-hour PG based on OGTT may be effective in distinguishing patients with a higher risk for MetS, which would be helpful in reducing the risk of adverse cardiovascular outcomes related to MetS.

It is known that patients with more baseline metabolic components are more likely to develop MetS than patients with fewer baseline metabolic components. Also in our study, the abnormal glycemic groups had worse metabolic profiles than the NGT groups, which suggests that abnormal glycemic groups had more baseline metabolic components. Thus, through subgroup analysis for the number of baseline metabolic components, we evaluated the risk of MetS according to 1-hour PG and 2-hour PG in patients with the same number of baseline metabolic components. Elevated PG levels markedly increased the risk of MetS even in patients with same number of baseline metabolic components, presenting the proportional relationship with MetS. This finding indicates that elevated PG level contributes to the increased risk for MetS, independently of the underlying metabolic state. Additionally, the development of MetS in patients with 0 or 1 metabolic components means that the aggravation of metabolic profiles occurred in two or more metabolic components during follow-up. Thus, it is suggested that the increase in PG level has an adverse impact not only on the development of MetS but also on deterioration of the metabolic milieu. Considering the effect of worse metabolic profiles on the pathogenesis of CVD, our results may provide a mechanism for studies observing the increased cardiovascular risk in IGT and elevated 1-hour PG (13, 24).

Another major finding of the study is in comparing the predictability of MetS between 1-hour PG and 2-hour PG. In our analysis, the H1N2 group had a higher risk of MetS than the N1H2 group. This result suggests that 1-hour PG is superior to 2-hour PG in predicting MetS, accompanying the higher potential cardiometabolic risk. Our analysis for AUC_{ROC} also presents the higher correlation of MetS with 1-hour PG than 2-hour PG. A DeLong test for the discovery sample showed a significantly higher AUC_{ROC} for 1-hour PG (0.576; 95% CI, 0.545 to 0.608) than for 2-hour PG (0.525; 95% CI, 0.493 to 0.557), which was identically observed in validation sample. Additionally, in an analysis for four subgroups defined by the optimal cutoff (142.5 mg/dL for 1-hour PG and 107.5 mg/dL for 2-hour PG) for our study participants, the H1N2 subgroup had a higher risk for MetS than N1H2 subgroup, identical to the subgroup analysis categorized by conventional cutoffs (155 mg/dL for 1-hour PG and 140 mg/dL for 2-hour PG). These results consistently indicate that 1-hour PG is superior to 2-hour PG in predicting incident MetS. Despite the scarcity of longitudinal study directly comparing the predictability of 1-hour PG and 2-hour PG for MetS, previous studies have also demonstrated higher predictability for 1-hour PG than for 2-hour PG in identifying metabolic risk factors. In longitudinal observations in the Botnia Study (16) and the San Antonio Heart Study (20), 1-hour PG correlated better with indices of insulin secretion and IR compared with 2-hour PG, and the predictive power of 1-hour PG evaluated by the AUC_{ROC} was greater than that of 2-hour PG. Additionally, cross-sectional studies for 94 overweight or obese Hispanics showed that fasting glucose, fasting insulin, and homeostatic model assessment of insulin resistance correlated better with 1-hour PG (r = 0.60, 0.47, and 0.52) than with 2-hour PG (r = 0.50, 0.41, and 0.45) (25). These results suggest that 1-hour PG was more closely associated with metabolic derangements than 2-hour PG. However, substantial evidence indicates that 1-hour PG exhibits the intermediate cardiometabolic risk profile between NGT with normal 1-hour PG and IGT, suggesting similar predictability (18, 27–30). Thus, our results do not ensure that 1-hour PG is a stronger predictor of cardiometabolic disease than 2-hour PG. Additional larger-scale studies should be conducted to determine which of 1-hour PG and 2-hour PG has greater impact on the development of cardiometabolic diseases, including MetS.

The merit of the study is the data obtained from a cohort of the general Korean population, including identifiable medical information and OGTT results at baseline and follow-up. Using the data, we could evaluate the relationship of 1-hour PG and 2-hour PG with incident MetS and compare their predictability for incident

MetS. Our results expand the clinical implications of 1-hour PG as a predictor for T2DM to identifying patients with higher risk for MetS. Nonetheless, it is not likely that our results are generalizable to other age and ethnic groups. All study participants were middle-aged Koreans without baseline MetS, IFG, and DM. These clinical features may create the difference between conventional cutoffs and our optimal cutoffs in our study participants. Additionally, the modest AUC_{ROC} of PG in our analysis (<0.6) may be explained by these features of our study participants. Thus, it is inferred that the cutoffs of PG and their predictability for MetS can vary according to clinical characteristics, including ethnicity, age, sex, and metabolic conditions.

In conclusion, our study showed a significant association of PG based on OGTT with incident MetS. Elevations of both 1-hour PG and 2-hour PG were significantly associated with the increased risk of MetS, which was similarly observed in NG patients. In particular, our findings suggest that 1-hour PG is superior to 2-hour PG in predicting MetS. Future longitudinal studies should investigate whether the increased risk of MetS indicated by elevated 1-hour PG actually links to cardiovascular morbidity and mortality.

Acknowledgments

Data in this study were from the KoGES (4851-302), National Research Institute of Health, Centers for Disease Control and Prevention, and Republic of Korea Ministry for Health and Welfare.

Author Contributions: S.K.P. coordinated the study, analyzed the data, and wrote the manuscript as a first author. J.-H.R. participated in conducting the study and writing the manuscript. C.-M.O. played a role in analyzing data and verifying the results. J.-M.C. participated in English editing and reviewing the manuscript. All authors had access to the data used in this study and participated in writing the manuscript. J.Y.J. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Correspondence and Reprint Requests: Ju Young Jung, MD, Total Healthcare Center, Kangbuk Samsung Hospital, 78 Saemunan-gil, Jongro-Gu, Seoul 110-746, Korea. E-mail: jjy0501@naver.com.

Disclosure Summary: The authors have nothing to disclose.

References

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr; International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;**120**(16):1640–1645.
2. O'Neill S, O'Driscoll L. Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev*. 2015;**16**(1):1–12.
3. Lim S, Shin H, Song JH, Kwak SH, Kang SM, Won Yoon J, Choi SH, Cho SI, Park KS, Lee HK, Jang HC, Koh KK. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998–2007. *Diabetes Care*. 2011;**34**(6):1323–1328.
4. Li R, Li W, Lun Z, Zhang H, Sun Z, Kanu JS, Qiu S, Cheng Y, Liu Y. Prevalence of metabolic syndrome in Mainland China: a meta-analysis of published studies. *BMC Public Health*. 2016;**16**(1):296.
5. Razak F, Anand SS, Shannon H, Vuksan V, Davis B, Jacobs R, Teo KK, McQueen M, Yusuf S. Defining obesity cut points in a multiethnic population. *Circulation*. 2007;**115**(16):2111–2118.
6. Wen CP, David Cheng TY, Tsai SP, Chan HT, Hsu HL, Hsu CC, Eriksen MP. Are Asians at greater mortality risks for being overweight than Caucasians? Redefining obesity for Asians. *Public Health Nutr*. 2009;**12**(4):497–506.
7. Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, Ko SH, Zimmet P, Son HY. Epidemic obesity and type 2 diabetes in Asia. *Lancet*. 2006;**368**(9548):1681–1688.
8. Hanley AJ, Karter AJ, Festa A, D'Agostino R Jr, Wagenknecht LE, Savage P, Tracy RP, Saad MF, Haffner S; Insulin Resistance Atherosclerosis Study. Factor analysis of metabolic syndrome using directly measured insulin sensitivity: the Insulin Resistance Atherosclerosis Study. *Diabetes*. 2002;**51**(8):2642–2647.
9. Meigs JB, Nathan DM, D'Agostino RB Sr, Wilson PW; Framingham Offspring Study. Fasting and postchallenge glycemia and cardiovascular disease risk: the Framingham Offspring Study. *Diabetes Care*. 2002;**25**(10):1845–1850.
10. Smith NL, Barzilay JI, Shaffer D, Savage PJ, Heckbert SR, Kuller LH, Kronmal RA, Resnick HE, Psaty BM. Fasting and 2-hour postchallenge serum glucose measures and risk of incident cardiovascular events in the elderly: the Cardiovascular Health Study. *Arch Intern Med*. 2002;**162**(2):209–216.
11. Meigs JB, Nathan DM, Wilson PW, Cupples LA, Singer DE. Metabolic risk factors worsen continuously across the spectrum of nondiabetic glucose tolerance. The Framingham Offspring Study. *Ann Intern Med*. 1998;**128**(7):524–533.
12. Rodriguez BL, Curb JD, Burchfiel CM, Huang B, Sharp DS, Lu GY, Fujimoto W, Yano K. Impaired glucose tolerance, diabetes, and cardiovascular disease risk factor profiles in the elderly. The Honolulu Heart Program. *Diabetes Care*. 1996;**19**(6):587–590.
13. Blake DR, Meigs JB, Muller DC, Najjar SS, Andres R, Nathan DM. Impaired glucose tolerance, but not impaired fasting glucose, is associated with increased levels of coronary heart disease risk factors: results from the Baltimore Longitudinal Study on Aging. *Diabetes*. 2004;**53**(8):2095–2100.
14. American Diabetes Association. Classification and diagnosis of diabetes. *Diabetes Care*. 2016;**39**(suppl 1):S13–S22.
15. Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? *Diabetes Care*. 2007;**30**(6):1544–1548.
16. 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**(2):281–286.
17. Alyass A, Almgren P, Akerlund M, Dushoff J, Isomaa B, Nilsson P, Tuomi T, Lyssenko V, Groop L, Meyre D. Modelling of OGTT curve identifies 1 h plasma glucose level as a strong predictor of incident type 2 diabetes: results from two prospective cohorts. *Diabetologia*. 2015;**58**(1):87–97.

18. Succurro E, Marini MA, Arturi F, Grembiale A, Lugarà 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**(1):245–249.
19. Jung JY, Oh CM, Ryoo JH, Choi JM, Choi YJ, Ham WT, Park SK. The influence of prehypertension, hypertension, and glycated hemoglobin on the development of type 2 diabetes mellitus in prediabetes: the Korean Genome and Epidemiology Study (KoGES). *Endocrine*. 2018;**59**(3):593–601.
20. 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**(8):1650–1655.
21. Park HS, Park CY, Oh SW, Yoo HJ. Prevalence of obesity and metabolic syndrome in Korean adults. *Obes Rev*. 2008;**9**(2):104–107.
22. Zeng P, Zhu X, Zhang Y, Wu S, Dong J, Zhang T, Wang S. Metabolic syndrome and the early detection of impaired glucose tolerance among professionals living in Beijing, China: a cross sectional study. *Diabetol Metab Syndr*. 2013;**5**(1):65.
23. Meigs JB, Williams K, Sullivan LM, Hunt KJ, Haffner SM, Stern MP, González Villalpando C, Perhanidis JS, Nathan DM, D'Agostino RB Jr, D'Agostino RB Sr, Wilson PW. Using metabolic syndrome traits for efficient detection of impaired glucose tolerance. *Diabetes Care*. 2004;**27**(6):1417–1426.
24. Wu X, Chen H, Wang Y, Li H. The relationship between coronary risk factors and elevated 1-h postload plasma glucose levels in patients with established coronary heart disease. *Clin Endocrinol (Oxf)*. 2013;**78**(1):67–72.
25. Joshipura KJ, Andriankaja MO, Hu FB, Ritchie CS. Relative utility of 1-h oral glucose tolerance test as a measure of abnormal glucose homeostasis. *Diabetes Res Clin Pract*. 2011;**93**(2): 268–275.
26. Kuang L, Huang Z, Hong Z, Chen A, Li Y. Predictability of 1-h postload plasma glucose concentration: a 10-year retrospective cohort study. *J Diabetes Investig*. 2015;**6**(6):647–654.
27. Marini MA, Succurro E, Frontoni S, Mastroianni S, Arturi F, Sciacqua A, Lauro R, Hribal ML, Perticone F, Sesti G. Insulin sensitivity, β-cell function, and incretin effect in individuals with elevated 1-hour postload plasma glucose levels. *Diabetes Care*. 2012;**35**(4):868–872.
28. Sesti G, Fiorentino TV, Succurro E, Perticone M, Arturi F, Sciacqua A, Perticone F. Elevated 1-h post-load plasma glucose levels in subjects with normal glucose tolerance are associated with unfavorable inflammatory profile. *Acta Diabetol*. 2014;**51**(6): 927–932.
29. Sciacqua A, Maio R, Miceli S, Pascale A, Carullo G, Grillo N, Arturi F, Sesti G, Perticone F. Association between one-hour postload plasma glucose levels and vascular stiffness in essential hypertension. *PLoS One*. 2012;**7**(9):e44470.
30. Sciacqua A, Miceli S, Carullo G, Greco L, Succurro E, Arturi F, Sesti G, Perticone F. One-hour postload plasma glucose levels and left ventricular mass in hypertensive patients. *Diabetes Care*. 2011; **34**(6):1406–1411.