

Postprandial C-peptide to glucose ratio as a predictor of β -cell function and its usefulness for staged management of type 2 diabetes

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Keywords

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ABSTRACT

Aims/Introduction: Type 2 diabetes is characterized by progressive deterioration of β -cell function. Recently, it was suggested that the C-peptide-to-glucose ratio after oral glucose ingestion is a better predictor of β -cell mass than that during fasting. We investigated whether postprandial C-peptide-to-glucose ratio (PCGR) reflects β -cell function, and its clinical application for management of type 2 diabetes.

Materials and Methods: We carried out a two-step retrospective study of 919 Korean participants with type 2 diabetes. In the first step, we evaluated the correlation of PCGR level with various markers for β -cell function in newly diagnosed and drug-naïve patients after a mixed meal test. In the second step, participants with well-controlled diabetes (glycated hemoglobin <7%) were divided into four groups according to treatment modality (group I: insulin, group II: sulfonylurea and/or dipeptidyl peptidase IV inhibitor, group III: metformin and/or thiazolidinedione and group IV: diet and exercise group).

Results: In the first step, PCGR was significantly correlated with various insulin secretory indices. Furthermore, PCGR showed better correlation with glycemic indices than homeostatic model assessment of β -cell function (HOMA- β). In the second step, the PCGR value significantly increased according to the following order: group I, II, III, and IV after adjusting for age, sex, body mass index and duration of diabetes. The cut-off values of PCGR for separating each group were 1.457, 2.870 and 3.790, respectively ($P < 0.001$).

Conclusions: We suggest that PCGR might be a useful marker for β -cell function and an ancillary parameter in the choice of antidiabetic medication in type 2 diabetes.

INTRODUCTION

Although many leading organizations emphasize individualized glycemic targets and treatment to lower glucose according to specific patient characteristics, the current algorithms of antihyperglycemic therapy in type 2 diabetes are based on treatment modality only considering the fasting and random blood glucose concentration, which are represented by glycated hemoglobin (HbA1c), in individual patients^{1–3}. It remains controversial to select first-line drugs to treat diabetic patients, even though metformin is a preferred first-line drug. In addition, there is no consensus to approach the most effective treatment

for an individual patient. Because most patients have already experienced substantial loss of β -cell function at the time of diagnosis of type 2 diabetes^{4,5}, it is more reasonable to select initial antidiabetic medications or modify drugs with consideration for β -cell function of individual patients.

Type 2 diabetes is characterized by insulin resistance and impaired insulin secretion⁶. Although insulin resistance shows little variation among patients with type 2 diabetes, pancreatic β -cell function declines progressively over time. The United Kingdom Prospective Diabetes Study (UKPDS) and the Belfast Diet Study have shown that progressive loss of β -cell function is a major cause of hyperglycemia and is also related to treatment failure of diabetes^{7,8}. In this regard, not only the evaluation of secular changes in insulin secretion, but also accurate methods to

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evaluate β -cell function are important for management of diabetes⁹. C-peptide, which is cleaved from insulin in secretory granules, is a well-known marker for β -cell function^{10,11}. In contrast to other indices for insulin secretion, C-peptide evaluation is able to assess β -cell function even in patients undergoing insulin therapy. Recently, it was suggested that the C-peptide-to-glucose ratio after oral glucose ingestion might be a better marker for pancreatic β -cell mass than fasting measures, such as the homeostatic model assessment of β -cell function (HOMA- β)¹¹.

Thus, we investigated the clinical significance of serum postprandial C-peptide-to-glucose ratio (PCGR) measurements in providing indices for insulin secretion and in discriminating treatment modalities for patients with type 2 diabetes.

MATERIALS AND METHODS

Patients and Study Design

Patients in the diabetes registry of Severance Diabetes Center between June 2009 and April 2011 were investigated in the present study. Type 2 diabetic patients aged older than 20 years were included. The exclusion criteria were severe liver or kidney disease, thyroid disorders, pregnancy, glucocorticoid therapy, heavy alcoholics and any malignancy including hematological disorders. Our investigation was a retrospective two-step study. In the first step, we investigated whether PCGR showed a significant correlation with indices for insulin secretion function, such as HOMA- β , as well as with indices for glycemic control. We analyzed 361 newly diagnosed type 2 diabetes patients who were drug-naïve, and had undergone a mixed meal test between June 2009 and April 2011. These participants included most of the patients described in our previous study¹². The test was a standardized liquid meal test (Ensure; Meiji Dairies Corporation, Tokyo, Japan; 500 kcal, 17.5 g fat [31.5%], 68.5 g carbohydrate [54.5%] and 17.5 g protein [14.0%]) after overnight fasting. Blood samples were collected at 0 and 90 min (basal and stimulated levels, respectively) for glucose, insulin and C-peptide analyses. We used fasting glucose, postprandial glucose, glycated albumin (GA) and HbA1c as the glycemic indices. For the insulin secretory indices, we used fasting or postprandial C-peptide (FCP or PCP), delta C-peptide (Δ CP), fasting C-peptide-to-glucose ratio (FCGR) or PCGR, insulinogenic index (IGI), index for C-peptide (ICI) and HOMA- β .

In the second step, we assessed the validity of PCGR as a predictor in the choice of antidiabetic therapy. For this, we analyzed 558 type 2 diabetic patients who achieved target glycemic control (HbA1c <7.0%), and had constant antidiabetic medication for at least 3 months between November 2009 and April 2011. The patients were analyzed retrospectively and divided into four groups according to their treatment modality (group I: exogenous insulin, group II: insulin secretagogues [sulfonylurea (SU) and/or dipeptidyl dipeptidase IV inhibitor (DPPiV)], group III: insulin sensitizer [metformin (Met) and/or thiazolidinedione (TZD)], and group IV: lifestyle modification [diet and exercise (D&E)]), based on the treatments'

strength and differential function on glycemic reduction. We first evaluated whether PCGR levels were significantly different among the groups. Subsequently, we investigated the cut-off values of PCGR for discriminating each medication group. To evaluate the validity of the cut-off values of PCGR, a training set comprising of randomly selected cases (70% of the participants) was used to select an optimal cut-off, which was then tested on the independent left-out validation set (30% of the participants). The blood samples for plasma glucose and C-peptide were obtained after an overnight fasting and 2 h after an individually composed breakfast. The study protocol was approved by the ethics committee of the Severance Hospital. According to the International Conference on Harmonization Good Clinical Practice (ICH GCP) guidelines¹³, all information was recorded in a manner so that participants could not be identified and kept in a locked computer.

Biochemical Test

Plasma glucose levels were measured using the glucose oxidase method and a Hitachi 747 automatic analyzer (Hitachi Instruments Service, Tokyo, Japan). Serum GA levels were measured using the enzymatic method and a Hitachi 7699 P module autoanalyzer (Hitachi Instruments Service, Tokyo, Japan). HbA1c levels were measured by high-performance liquid chromatography using a Variant II Turbo (Bio-Rad Laboratories, Hercules, CA, USA). Serum insulin and C-peptide levels were measured in duplicate by immunoradiometric assay (Beckman Coulter, Fullerton, CA, USA). Δ CP was calculated as (C-peptide 90 min – C-peptide 0 min). HOMA- β was calculated as fasting insulin (μ IU/mL) \times 20 / fasting glucose (mmol/L) – 3.5. The IGI was calculated as (insulin 90 min – insulin 0 min) / (glucose 90 min – glucose 0 min), while the corresponding ICI was (C-peptide 90 min – C-peptide 0 min) / (glucose 90 min – glucose 0 min). FCGR and PCGR were calculated as (fasting or postprandial C-peptide level [ng/mL] / fasting or postprandial glucose level [mg/dL] \times 100).

Statistical Analysis

Analysis of variance (ANOVA) or analysis of covariance (ANCOVA) tests was used to compare variables. All continuous variables are shown as the mean \pm standard deviation except for ANCOVA analysis (mean \pm standard error). To compare the relationship among HbA1c, GA and other variables, Pearson's correlation coefficients were used to assess the associations between clinical and laboratory variables. We analyzed the differences in the correlated coefficients between PCGR or HOMA- β and glycemic indices using Steiger's Z-test. The receiver operating characteristic (ROC) curve of PCGR was shown, and the area under the curve (AUC) was calculated for separating each medication group. To determine the optimal cut-off value, the point on the ROC curve with maximum Youden index (sensitivity + specificity – 1) was calculated. Statistical analyses were carried out using SAS version 9.2 (SAS Institute, Cary, NC, USA). A *P*-value <0.05 was considered significant.

RESULTS

Correlations Between Variable Indices of β -Cell Function

The baseline characteristics of the newly diagnosed type 2 diabetic patients are shown in Table 1. From the first step analysis, the correlation between PCGR and insulin secretory indices widely accepted as predictors for β -cell function was investigated in 361 drug-naïve patients with newly presenting type 2 diabetes (Table 2). Among these indices, PCP, Δ CP and PCGR showed a significant correlation with previously established insulin secretory indices, such as IGI, ICI and HOMA- β . The PCGR showed a stronger correlation with HOMA- β ($r = 0.552$, $P < 0.001$) than PCP and Δ CP ($r = 0.370$, $r = 0.307$, respectively, all $P < 0.001$). Although FCGR had a moderately strong correlation (0.6–0.8) with HOMA- β ($r = 0.705$, $P < 0.001$), FCGR did not have any correlation with IGI or ICI. As expected, IGI showed a very strong correlation (at least 0.8) with ICI ($r = 0.928$, $P < 0.001$). However, neither IGI nor ICI showed any correlation with HOMA- β . A partial correlation adjusted for age, sex and body mass index (BMI) showed similar results among various insulin secretory indices.

Correlations of PCGR and HOMA- β with Glycemic Indices

During the first step analysis to find an effective insulin secretory index predicting well-controlled glycemia, we compared the correlations of indices for insulin secretion, such as PCGR or HOMA- β , with various glycemic indices, such as fasting and postprandial glucose, glycated albumin and HbA1c.

Table 1 | Characteristics of 361 newly diagnosed, drug-naïve type 2 diabetic patients

Variables	
Male:female	140:221
Age (years)	55.3 \pm 11.0
BMI (kg/m ²)	25.24 \pm 3.39
HbA1c (%)	7.3 \pm 1.8
Glycated albumin (%)	17.8 \pm 7.3
FPG (mg/dL)	127.3 \pm 42.4
PPG (mg/dL)	197.1 \pm 86.5
FCP (ng/mL)	2.23 \pm 0.82
PCP (ng/mL)	6.78 \pm 3.11
Δ CP	4.57 \pm 2.88
FCGR	1.86 \pm 0.75
PCGR	3.99 \pm 2.14
IGI	1.14 \pm 3.16
ICI	0.11 \pm 0.31
HOMA- β	59.35 \pm 31.82

Δ CP, postprandial C-peptide; BMI, body mass index; FCGR, fasting C-peptide-to-glucose ratio; FCP, fasting C-peptide; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HOMA- β , homeostasis model assessment of β -cell function; ICI, C-peptide-genic index; IGI, insulinogenic index; PCGR, postprandial C-peptide-to-glucose ratio; PCP, postprandial C-peptide; PPG, postprandial plasma glucose.

Overall, both indices showed a good correlation with glycemic indices (Figure 1). Although PCGR was calculated using postprandial indices, including C-peptide and glucose level, PCGR ($r = -0.558$, $P < 0.001$) showed a strong correlation with fasting glucose levels, which was shown in HOMA- β ($r = -0.587$, $P < 0.001$). Additionally, PCGR showed significantly stronger correlations with GA and HbA1c ($r = -0.602$ with GA and $r = -0.591$ with HbA1c, all $P < 0.001$) than HOMA- β did ($r = -0.521$ with GA, and $r = -0.471$ with HbA1c, all $P < 0.001$).

Clinical Characteristics of Participants According to Antidiabetic Medications

In the second step analysis, we hypothesized that the patients who had achieved target glycemic control (HbA1c <7%) might have received appropriate antidiabetic therapy according to their β -cell secretory function. To investigate whether PCGR can differentiate treatment modalities in type 2 diabetes, we analyzed 558 patients with type 2 diabetes under good glycemic control (HbA1c <7%). Table 3 shows the significantly different fasting and postprandial glucose levels among groups that were divided according to treatment modalities. As expected, the insulin-treated group I showed lower C-peptide level (both FCP and PCP) and longer duration of disease than the other medication groups. In contrast to FCGR level, mean PCGR levels were significantly different among groups, and decreased according to the following order: group IV (D&E), group III (Met/TZD), group II (SU/DPPiVi) and group I (insulin; Table 3 and Figure 2). The different PCGR levels among groups were still significant after adjusting for age, sex, BMI and duration of disease (Figure 2).

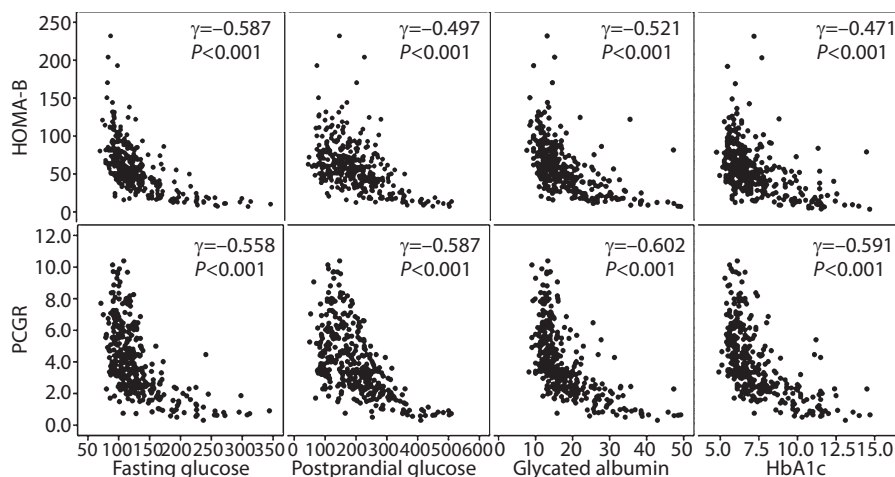
Cut-off Values of PCGR for Discriminating Antidiabetic Medication groups

We hypothesized that different types of treatment modalities could be differentiated by PCGR levels in patients with good glycemic control, and determined the cut-off values of PCGR for distinguishing between treatment modalities, such as SU/DPPiVi, Met/TZD and D&E. From the training set (70% of the participants), the PCGR cut-off value for discriminating between group I (insulin) and group II (SU/DPPiVi) was 1.457 (AUC 0.763, 95% confidence interval [CI] 0.67–0.86) with 92.6% sensitivity and 60.0% specificity; between group II (SU/DPPiVi) and group III (Met/TZD) was 2.870 (AUC 0.634, 95% CI 0.58–0.69) with 75.5% sensitivity and 51.4% specificity; between group III (Met/TZD) and group IV (D&E) was 3.790 (AUC 0.593, 95% CI 0.53–0.66) with 69.5% sensitivity and 49.1% specificity (Figure 3 and Supplementary Table 1). In the validation set (the remaining 30% of the participants), the sensitivity and specificity of PCGR cut-off value were 81.0% and 41.7% between group I (insulin) and group II (SU/DPPiVi), 73.9% and 44.4% between group II (SU/DPPiVi) and group III (Met/TZD), and 70.5% and 52.2% between group III (Met/TZD) and group IV (D&E), respectively.

Table 2 | Correlation between postprandial C-peptide-to-glucose ratio and insulin secretory indices

	FCP	PCP	ΔCP	FCGR	PCGR	IGI	ICI	HOMA-β
FCP	—	0.419**	0.169*	0.788**	0.198**	0.085	0.037	0.319**
PCP		—	0.967**	0.506**	0.732**	0.218**	0.180**	0.370**
ΔCP			—	0.313**	0.742**	0.212**	0.181**	0.307**
FCGR				—	0.538**	0.103	0.080	0.705**
PCGR					—	0.277**	0.256**	0.552**
IGI						—	0.928**	0.082
ICI							—	0.094
HOMA-β								—
FCP†	—	0.392**	0.155*	0.757**	0.196**	0.047	0.014	0.280**
PCP†		—	0.970**	0.489**	0.738**	0.212**	0.171*	0.357**
ΔCP†			—	0.324**	0.740**	0.215**	0.180*	0.309**
FCGR†				—	0.557**	0.075	0.062	0.706**
PCGR†					—	0.276**	0.256**	0.561**
IGI†						—	0.929**	0.064
ICI†							—	0.085
HOMA-β†								—

* $P < 0.01$, ** $P < 0.001$, derived from Pearson's correlation. †Pearson's partial correlation adjusted for age, sex and body mass index. ΔCP, postprandial C-peptide; FCGR, fasting C-peptide-to-glucose ratio; FCP, fasting C-peptide; HOMA-β, homeostasis model assessment of β-cell function; ICI, C-peptide-genic index; IGI, insulinogenic index; PCGR, postprandial C-peptide-to-glucose ratio; PCP, postprandial C-peptide.

**Figure 1** | Correlations between postprandial C-peptide-to-glucose ratio (PCGR) or homeostatic model assessment of β-cell function (HOMA-β) and glycemic indices. HbA1c, glycated hemoglobin.

DISCUSSION

Insulin resistance is observed in more than 80% of type 2 diabetes patients with little variation¹⁴. In contrast, pancreatic β-cell mass decreases progressively during the course of diabetes, which results in significantly decreased insulin secretory capacity^{7,15,16}. Because glucose control in diabetes is closely associated with pancreatic β-cell mass, it is important to identify predictors of pancreatic β-cell function in patients with type 2 diabetes. In Asian populations, inadequate β-cell response to increasing insulin resistance is considered as the cause of loss of glycemic control and increased risk of diabetes, even with

relatively little weight gain¹⁷. For this reason, the typical characteristic of Korean patients with type 2 diabetes in the development and aggravation of hyperglycemia is secretory β-cell dysfunction¹⁸. The oral glucose tolerance test and HOMA indices have been commonly applied as functional tests for insulin secretion^{19,20}. However, the interpretation of insulin concentrations is complicated, because insulin levels should be not only matched with glucose concentrations, but also borne in mind in the situation of insulin use. Although HOMA is often used in large clinical and epidemiological studies, it is not suitable for some diabetic patients because of hyperglycemic state or

Table 3 | Characteristics of 558 patients with well controlled glycemia according to medication groups

	Group I (Insulin)	Group II (SU/DPPIV)	Group III (Met/TZD)	Group IV (D&E)	P-value†
n	42	211	156	149	
Male : female	32:10	105:106*	86:70*	86:63*	0.016
Age (years)	60.0 ± 13.5	65.7 ± 9.8*	63.0 ± 10.2§	58.5 ± 10.3§¶	<0.001
BMI (kg/m ²)	23.22 ± 2.90	24.37 ± 2.94*	24.91 ± 3.03*	24.21 ± 3.37	0.021
Duration	8.8 ± 1.5	7.2 ± 0.6*	6.4 ± 0.5*§	4.1 ± 0.3*§¶	<0.001
HbA1c (%)	8.02 ± 2.05	7.12 ± 1.46*	6.73 ± 0.86*§	6.17 ± 0.48*§¶	<0.001
HbA1c (%)‡	6.5 ± 0.4	6.4 ± 0.4	6.5 ± 0.3	6.3 ± 0.4*§¶	<0.001
FPG (mg/dL)	140.8 ± 69.1	128.4 ± 38.7*	119.5 ± 25.0*§	112.6 ± 18.8*§	<0.001
PPG (mg/dL)	238.6 ± 116.2	209.5 ± 69.7*	174.1 ± 49.0*§	154.1 ± 47.1*§¶	<0.001
FCP (ng/mL)	1.34 ± 1.23	2.17 ± 0.93*	2.20 ± 1.14*	2.06 ± 0.83*	<0.001
PCP (ng/mL)	3.32 ± 1.99	6.03 ± 2.62*	6.75 ± 2.69*§	6.91 ± 2.45*§	<0.001
FCGR	1.12 ± 1.27	1.82 ± 0.92*	1.94 ± 1.32*	1.85 ± 0.77*	<0.001
PCGR	1.63 ± 1.25	3.17 ± 1.61*	4.05 ± 1.61*§	4.71 ± 1.67*§¶	<0.001

* $P < 0.05$ vs insulin group. † P -values by χ^2 -test or ANOVA are provided for the four-group comparisons. ‡Glycated hemoglobin (HbA1c) when achieved target glycemic control (HbA1c <7%). § $P < 0.05$ vs sulfonylurea/dipeptidyl peptidase IV inhibitor (SU/DPPIV) group. ¶ $P < 0.05$ vs metformin/thiazolidinedione (Met/TZD) group. CGR, fasting C-peptide-to-glucose ratio; D&E, diet and exercise; F/U, follow up; FCP, fasting C-peptide; FPG, fasting plasma glucose; PCGR, postprandial C-peptide-to-glucose ratio; PCP, postprandial C-peptide; PPG, postprandial plasma glucose.

insulin use. In addition, a recent study measuring β -cell area in humans showed that there was no relationship between HOMA- β and β -cell area¹¹.

Postprandial insulin deficiency is regarded as the main explanatory factor of deteriorating glucose control in newly developed type 2 diabetes²¹. A study showed that the reduction of postprandial insulin secretion is more prominent than that of fasting insulin secretion in the progression of type 2 diabetes²². It was thus suggested that postprandial β -cell function might be a more important factor for glycemic control than fasting β -cell function. Although there are many studies on indices for insulin secretory function, only a few studies have investigated staged management of type 2 diabetes based on insulin secretory function using these indices. Furthermore, the studies were only able to distinguish which patients require insulin therapy based on the indices^{23,24}. Recently, PCGR after oral glucose ingestion was suggested to be a better predictor for the β -cell area, the region responsible for β -cell function, than fasting measures¹¹. Therefore, we used a new, expanded practical index, PCGR, for assessing insulin secretion as part of a new therapeutic strategy for individualized treatment for type 2 diabetes. To precisely analyze the relationship between endogenous insulin secretion and the various markers, we carried out a standardized mixed meal test in newly diagnosed, drug-naïve type 2 diabetic patients. PCGR values were correlated with other insulin secretory indices, such as HOMA- β , IGI and ICI (Table 2). Additionally, PCGR showed a strong correlation with glycemic indices including plasma glucose level and glycated index for glycemic control (HbA1c and GA) than HOMA- β (Figure 1). These results suggest that PCGR might be used as an index for insulin secretion in practical fields. In addition, PCGR is easily calculated using postprandial

C-peptide and glucose levels measured at the time of diagnosis for type 2 diabetic patients.

In the present study, we categorized diabetic patients with good glycemic control based on their maintained antidiabetic medication. As shown in Figure 2, PCGR levels after adjusting for age, sex, BMI and duration of disease were different according to the medication group (2.27 ± 0.28 , 3.32 ± 0.11 , 3.89 ± 0.13 , 4.53 ± 0.14 for group I (insulin), group II (SU/DPPIV), group III (Met/TZD) and group IV (D&E), respectively, $P < 0.001$ for ANCOVA). We also obtained the cut-off values of PCGR to distinguish each treatment group in patients with well-controlled glycemic level from the training set and verified that in the validation set. From the analysis of the training set, the cut-off values of PCGR for discriminating between treatment groups were 1.457, 2.870 and 3.790, respectively (all $P < 0.001$; Figure 3). In the validation set, the sensitivity of the PCGR cut-off value was maintained as relatively constant, although the specificity of that was low. We suggest that these cut-off values could be applied when choosing antidiabetic agents for patients with type 2 diabetes. In accordance with the present results, recent studies have shown that PCGR is also a better predictor of future insulin therapy than fasting C-peptide index^{25,26}. PCGR is a simple and practical marker for insulin secretion, and it can be helpful in determining appropriate treatment modalities, such as insulin, insulin secretagogues (SU and/or DPPIV), insulin sensitizer (Met and/or TZD) and lifestyle modification. As plasma glucose is the most potent stimulator of insulin secretion, it is presumed that PCGR level reflects β -cell function more precisely than FCGR or plasma C-peptide level itself does. Furthermore, insulin secretion is more impaired in the postprandial state than in the fasting state⁷, and it is stimulated by high plasma glucose level and incretin hormone²⁷. Thus, PCGR index might be a more useful

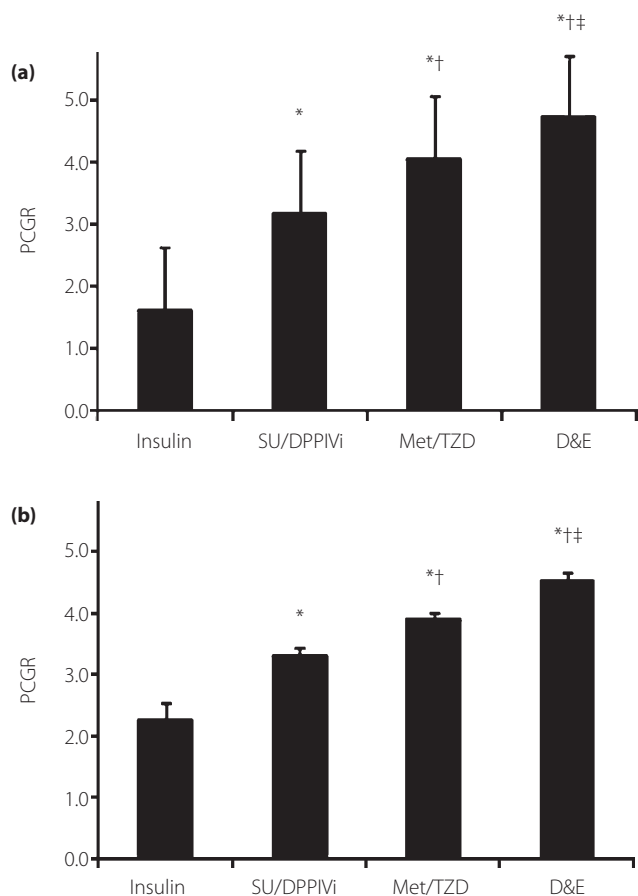


Figure 2 | Mean postprandial C-peptide-to-glucose ratio (PCGR) levels in the patients according to medication groups (a) before and (b) after adjusting for age, body mass index, and duration of diabetes. * $P < 0.05$ vs insulin group; † $P < 0.05$ vs sulfonylurea/dipeptidyl peptidase IV inhibitor (SU/DPPiVi) group; ‡ $P < 0.05$ vs metformin/thiazolidinedione (Met/TZD) group. D&E, diet and exercise.

predictor of β -cell function than other indices measured during the fasting state.

The limitations of the present study were as follows. First, the study was based on retrospective analysis. Based on the results from the present study, a prospective study is in progress. Second, we did not examine glucagon-stimulated C-peptide levels, which is one of the most widely used methods for insulin secretory functions of diabetic patients^{28,29}. In addition, the C-peptide levels could have been influenced or modified by the medications in the second step analysis. For instance, prolonged treatment with sulfonylurea could have reduced C-peptide, whereas prolonged treatment with TZD could have increased β -cell mass. For this reason, a prospective study of drug-naïve patients is in progress, based on PCGR value. Third, we did not include meglitinide in the present study, although we suggest the use of similar cut-off values of PCGR as in group II (SU/DPPiVi), especially for patients with high postprandial glucose. Fourth, we could not

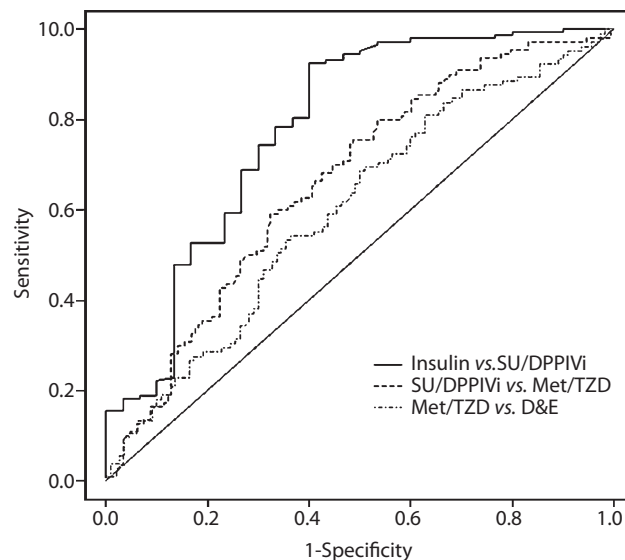


Figure 3 | Receiver operating characteristic (ROC) curves of postprandial C-peptide-to-glucose ratio (PCGR) for classifying each medication group. Area under the curve (AUC) of 0.763 (95% confidence interval [CI] 0.671–0.855) for group I (insulin) vs group II (sulfonylurea/dipeptidyl peptidase IV inhibitor [SU/DPPiVi]), 0.634 (95% CI 0.577–0.691) for group II (SU/DPPiVi) vs group III (metformin/thiazolidinedione [Met/TZD]) and 0.593 (95% CI 0.529–0.658) for group III (Met/TZD) vs group IV (diet and exercise [D&E]). The cut-off values of PCGR were 1.457 with 92.6% sensitivity and 60.0% specificity for group I (insulin) vs group II (SU/DPPiVi), 2.870 with 75.5% sensitivity and 51.4% specificity for group II (SU/DPPiVi) vs group III (Met/TZD), and 3.790 with 69.5% sensitivity and 49.1% specificity for group III (Met/TZD) vs group IV (D&E).

separately assess the additional effects of insulin sensitizer (Met or TZD) in group I (insulin) or group II (SU/DPPiVi), although 76.4% of patients in the present study had already been treated with additional insulin sensitizers, such as Met or TZD. Finally, the different cut-off values of PCGR should be investigated in different ethnic populations. Despite these limitations, we were able to differentiate treatment modalities of well-controlled type 2 diabetic patients with PCGR, and this value can be a useful marker in the determination of antidiabetic therapy.

In conclusion, the PCGR index might be used as a marker of insulin secretion and be used as an ancillary parameter for selecting antidiabetic medication, as well as insulin therapy in type 2 diabetic patients, based on their individual β -cell functions. Further prospective study will be warranted to assess the usefulness of the PCGR index for staged diabetic management.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1 | Cut-off values of postprandial C-peptide-to-glucose ratio (PCGR) for discriminating each medication group in the training (randomly selected 70% of the participants) and validation (the remaining 30% of the participants) set.