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Do Static and Dynamic Insulin Resistance Indices Perform Similarly in Predicting Pre-diabetes and Type 2 Diabetes?

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Abstract

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Aims—We designed a study to compare the predictive power of static and dynamic insulin resistance indices for categorized pre-diabetes (PDM) / type 2 diabetes (DM).

Methods—Participants included 1,134 adults aged 18-60 years old with normal glucose at baseline who completed both baseline and 6-years later follow-up surveys. Insulin resistance indices from baseline data were used to predict risk of PDM or DM at follow-up. Two static indices and two dynamic indices were calculated from oral glucose tolerance test results (OGTT) at baseline. Area under the receiver operating characteristic curve (AROC) analysis was used to estimate the predictive ability of candidate indices to predict PDM/DM. A general estimation equation (GEE) model was applied to assess the magnitude of association of each index at baseline with the risk of PDM/DM at follow-up.

Results—The dynamic indices displayed the largest and statistically predictive AROC for PDM/DM diagnosed either by fasting glucose or by postprandial glucose. The bottom quartiles of the dynamic indices were associated with an elevated risk of PDM/DM vs. the top three quartiles. However, the static indices only performed significantly to PDM/DM diagnosed by fasting glucose.

Conclusions—Dynamic insulin resistance indices are stronger predictors of future PDM/DM than static indices. This may be because dynamic indices better reflect the full range of physiologic disturbances in PDM/DM.

Keywords

insulin resistance indices; predict; pre-diabetes; type 2 diabetes; Chinese; twin; adult

Introduction

Insulin resistance (IR) is typically defined as decreased sensitivity or responsiveness to the metabolic action of insulin, such as insulin-mediated glucose disposal and inhibition of hepatic glucose production. Insulin resistance plays a major pathophysiological role in the development of type 2 diabetes (DM)[1]. Both ß-cell dysfunction and insulin resistance can be detected long before type 2 diabetes and pre-diabetes (PDM) within individuals with a family history of diabetes [2]. Therefore, the ability to accurately measure IR may enable the prediction of those at risk for PDM and DM and assist with targeted interventions.

IR can be quantified using detailed physiological protocols, such as the hyperinsulinemic-euglycemic clamp technique[3]. This method, however, is complicated, invasive and costly for use in large epidemiological studies. Accordingly, a number of surrogate indices have been proposed to estimate IR in large numbers of subjects[4]. These indices are formulated using static and dynamic insulin and glucose measurements during a glucose tolerance test (OGTT), and the criterion validity of these measurements has been demonstrated in various populations[4]. Although several studies have reported the degree to which these indices are able to predict DM in prospective analyses and have discovered a disparity in their predictive ability for DM [5-7], little research has been conducted to explore the reasons for such disparity. Given that the diagnostic criteria of DM embraces two glucose cutoffs, fasting and stimulated glucose concentrations, the predictive ability of IR indices may be dependent on the strength of their correlation with elevated fasting or stimulated glucose

concentration at diagnosis. Thus, in predicting PDM/DM, those indices that correlate well with both glucose concentrations would perform better than other indices that correlate well with just one glucose concentration. However, this hypothesis has never been tested. The large dataset of the Anqing Twin Cohort, which includes data for OGTT at both baseline and follow-up and allows for the formulation of insulin sensitivity indices at baseline and categorization of PDM/DM at follow-up, provides a unique opportunity to investigate this hypothesis. We selected two static and two dynamic IR indices from a previous study[6] that exhibited the best predictive ability for DM, and compared their powers to predict categorized PDM/DM using longitudinal data from the Anqing Twin Cohort Study.

Methods and Procedures

Study Sample

We used data from the longitudinal Anqing Twin Cohort Study, which has been previously described [8]. Briefly, a baseline survey was carried out in eight rural counties of Anqing from 1998-2000; and follow-up data were collected from 2005-2006. OGTT was administrated at both the baseline and follow-up examination for diagnosis of PDM/DM. In addition, participants were invited to a central office to complete an interview-based questionnaire and physical exam at both times. Subjects were included in the present study if they met the following criteria: 1) age≥18 at baseline; 2) without reported or diagnosed DM/PDM by OGTT at baseline; and 3) complete OGTT at both time points. After the exclusion of 10 subjects with outlier values (outside ±3 standard deviation) for insulin resistance indices, 1,134 subjects were eligible for this proposed study. The study protocol was approved by the Institutional Review Boards of Ann & Robert H. Lurie Children's Hospital of Chicago (formerly Children's Memorial Hospital), Chicago, USA and the Institute of Biomedicine, Anhui Medical University, Hefei, China. All participants gave written consent.

Anthropometric measures

Height was measured without shoes to the nearest 0.1 cm on a portable stadiometer. Weight was measured without shoes to the nearest 0.1 kg with the subject standing motionless in the center of a calibrated scale. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Definition of insulin resistance/sensitivity indices and PDM/DM

OGTT was conducted using standard procedures (WHO, 1985) in all subjects. A 75 g oral glucose equivalent load was administered after a 12-14 hour fast. Blood specimens were obtained at 0hs and 2hs for determination of plasma glucose and serum insulin concentration. Laboratory assay methods have been described previously [9]. We selected four IR indices with the best predictive ability for DM from a previous study[6] that assessed 19 IR indices in a multiethnic population. Definitions of the IR indices for QUICKI[10], ISIgly_b[11], SiM[12] and $ISI_{0,120}$[13] are presented in Table 2. Among these indices, QUICKI and ISIgly_b are considered to be static indices because they are calculated using fasting glucose and insulin measures while SiM and $ISI_{0,120}$ are considered to be

dynamic indices because they use both fasting and postprandial glucose and insulin measures.

DM was diagnosed based on OGTT results with fasting plasma glucose (FPG) ≥7.0mmol/L and/or 2-h plasma glucose (2HPG) ≥11.1 mmol/L. Subjects diagnosed with DM were grouped into the following three categories:

1. DM diagnosed only by fasting glucose;
2. DM diagnosed only by postprandial glucose; and
3. DM diagnosed by both fasting and postprandial glucose.

Pre-diabetes (PDM) was also based on WHO criteria[14] with FPG ≥6.1 and <7.0 mmol/L and 2HPG ≥7.8 and <11.1 mmol/L. Subjects diagnosed with PDM were grouped into the following three categories:

1. Isolated impaired fasting glucose (IFG);
2. Isolated impaired glucose tolerance (IGT);
3. Combined IFG and IGT (IFG&IGT).

Statistical methods

The distribution of insulin and SiM were positively skewed and logarithmically transformed to normalize the data for statistical analyses. Univariate analysis included the chi-squared test for categorical variables and the t-test for continuous variables. Pearson's correlation coefficients were calculated to relate each insulin resistance index versus fasting and postprandial glucose levels at follow-up. We used the gender-specific Z-score of each IR index to calculate the area under the receiver operating characteristic (AROC) curve for the models. The magnitude of association of each index at baseline with the risk of PDM/DM at follow-up was assessed by comparing the risk of those in the gender-specific bottom quartile versus those in the gender-specific top quartiles. To account for the intra-twin correlation, we fitted general estimating equations (GEE) in all logistic regression models. Regression analyses were performed for all subjects first, and then repeated for strata based on the diagnostic definition for PDM/DM. In stratified analysis, isolated IFG and DM diagnosed only by fasting glucose were merged into one group (PDM/DM by fasting glucose) while isolated IGT and DM diagnosed only by postprandial glucose were merged into another group (PDM/DM by postprandial glucose). Combined IFG&IGT and DM were included into each group above as they possess both fasting and postprandial abnormal glucose. All analyses were performed using SAS software, version 9.2 (SAS Institute, Cary, NC, USA).

Results

The demographic and clinical characteristics of subjects in this study are summarized in Table 1. In total, 658 male and 485 female adults aged 18-60 at baseline were included in this study. At baseline, males were older and had lower BMI and postprandial glucose than females ($p<0.01$). Males also had both lower fasting and postprandial insulin measures than females ($p<0.01$). There was no significant gender difference in fasting glucose. At follow-

up, postprandial glucose in females was significantly higher than in males ($p<0.01$). The proportion of diagnosed PDM/DM was not different between genders.

We found that the dynamic indices, $ISI_{0,120}$ and SiM, were strongly correlated with both fasting glucose and postprandial glucose at follow-up (r: |0.12-0.16|, $p<0.0001$) whereas the static indices, ISIgly_b and QUICKI, were correlated with fasting glucose (r:|0.10| and |0.12|, $p<0.0001$ and $p=0.0004$, respectively). Only ISIgly_b was less strongly associated with postprandial glucose (Table 2).

AROC analysis results are presented in Table 3. The dynamic indices predicted PDM/DM either determined by fasting or postprandial glucose. The AROC of $ISI_{0,120}$ (0.61, 95% CI: 0.56-0.66 for whole PDM/DM; 0.66, 95% CI: 0.60-0.72 for PDM/DM determined by fasting glucose; 0.60, 95% CI: 0.56-0.66 for PDM/DM determined by postprandial glucose) ranked the highest amongthe four studied indices. In contrast, the static indices only predicted PDM/DM determined by fasting glucose, with an AROC of 0.57(95%CI: 0.51-0.64) for both indices.

The magnitude of association for each insulin resistance index at baseline with the risk of PDM/DM at follow-up (Table 4) was similar that from the AROC analysis. Subjects (Supplemental Figure) in the bottom quartile of $ISI_{0,120}$ and SiM at baseline were more likely to develop PDM/DM at follow-up than others (23.5% vs.12.4%; 21.8% vs. 11.9%, respectively). In contrast, there was no significant association with ISIgly_b or QUICKI. As compared to the top three quartiles, the bottom quartile of the dynamic indices, $ISI_{0,120}$ or SiM, at baseline was associated with an increased risk of PDM/DM at follow-up (OR: 2.4, 95%CI: 1.3-2.4 and OR: 1.8 95%CI: 1.3-2.6, respectively). In contrast, baseline values for the static indices, ISIgly_b and QUICKI, showed no association with PDM/DM at follow-up. In stratified analyses (Table 3), the association of the baseline dynamic indices, $ISI_{0,120}$ and SiM, with PDM/DM at follow-up remained in each subset. However, the bottom quartile of the static indices, ISIgly_b and QUICKI, showed a significant association with PDM/DM only when diagnosed by fasting glucose level (OR:1.9, 95%CI:1.2-3.0 for both).

Discussion

To our knowledge, this is the first study to assess the comparative ability of IR indices to predict PDM/DM stratified by diagnostic criteria. Our results show that dynamic indices ($ISI_{0,120}$ and SiM) are superior to static indices (ISIgly_b and QUICKI) as predictors of future PDM/DM. This superiority is based on the strong correlation of $ISI_{0,120}$ and SiM with either fasting or postprandial glucose at follow-up, which was not found for the static indices, ISIgly_b or QUICKI. The findings in this study yield intriguing patterns with regard to the difference in predictive ability of insulin resistance indices in categorizing PDM/DM, which has never been reported in previous studies. Moreover, the strength by which the IR indices correlated to the fasting or stimulated glucose levels was confirmed to be responsible for such difference.

A few prior population-based studies [5-7] have investigated and compared the ability of insulin resistance indices to predict future diabetes diagnosed by OGTT result. Yet, these

studies did not include PDM as an outcome, and there has been even less exploration of the potential disparity in their predictive ability for different diagnostic criteria of PDM/DM. In two of these studies [5, 6], IR indices derived from fasting glucose and insulin alone performed similarly in predicting diabetes as compared to other indices utilizing both fasting and stimulated measures of insulin and glucose. Hanley and his colleagues compared 19 IR indices and discovered that ISIgly_b, QUICKI, SiM and $ISI_{0,120}$ displayed stronger associations with the incidence of diabetes than other IR indices[6]. Their study found $ISI_{0,120}$ to be the strongest predictor of DM, which is consistent with our findings. However, they did not further explore if these indices had the same power to predict PDM/DM diagnosed by different criteria.

Our research furthered this previous study in a Chinese sample population. We selected the top two best predictors respectively from among the static, $ISI_{0,120}$ and SiM, and dynamic, ISIgly_b and QUICKI, indices to evaluate their predictive ability. Moreover, we explored the reasons for the differences in their predictive ability. Taking advantage of OGTT data at both time points in our study, we extended the results from previous research in two ways: 1) we assessed the predictive ability of IR indices for both DM and PDM; and 2) we stratified the diagnosis of PDM/DM into two types: diagnosed by fasting glucose or diagnosed by postprandial glucose. From the study findings, we discovered that the dynamic IR indices, $ISI_{0,120}$ and SiM, whose formulas include both fasting and stimulated glucose and insulin concentrations, show superior performance in predicting PDM/DM at follow-up regardless of whether PDM/DM was characterized by elevated fasting or stimulated concentration. In contrast, the static indices, ISIgly_b and QUICKI, whose formulas only include fasting glucose and insulin concentration, were only predictive of PDM/DM determined by high fasting glucose concentration.

The epidemiological differences between IFG and IGT indicate that different pathophysiologic mechanisms may contribute to a disturbance in glucose homeostasis [15, 16]. Although both isolated IFG and isolated IGT are insulin-resistant states, they differ in terms of the site of insulin resistance[17]. People with isolated IFG predominantly have hepatic insulin resistance and normal skeletal muscle insulin sensitivity, whereas individuals with isolated IGT have normal to slightly reduced hepatic insulin resistance and moderate to severe skeletal muscle insulin resistance. Not surprisingly, individuals with combined IFG and IGT manifest both skeletal muscle and hepatic insulin resistance. In the fasting state, the majority (70-75%) of glucose uptake occurs in insulin-insensitive tissues[18] and >75% endogenous glucose production originates in insulin-sensitive liver tissue[19]. As a result, insulin resistance indices derived from fasting glucose and insulin mainly reflect hepatic insulin sensitivity, whose deterioration eventually results in IFG or DM diagnosed only by elevated fasting glucose. After an oral glucose load, the ensuing hyperglycemia and hyperinsulinemia work together to suppress hepatic glucose production and stimulate glucose uptake by the splanchnic (liver) and peripheral (muscle) tissue[10, 20]. Stimulated glucose concentration is the result of insulin's action on both liver and muscle tissue. Therefore, dynamic indices, including both fasting and stimulated glucose and insulin, reflect hepatic as well as peripheral IR. Since dynamic indices capture two aspects of the pathophysiology of PDM/DM, hepatic and muscular insulin resistance, it is unequivocal that these indices would perform superiorly to static indices in predicting PDM/DM.

There are several limitations to this study. First, since the subjects in our study are from a twin population, we could not treat them as truly independent participants. To address this issue, we fitted a GEE model to account for intra-twin correlation. Second, due to the very low incidence of DM in this sample, precisely assessing the predictive ability of insulin resistance for only DM was not feasible. Future research in a large sample with a greater prevalence of DM is needed to explore this question more precisely. Third, some studies support that impaired ß cell function is also involved in the pathogenesis of PDM/DM[21, 22], but we could not explore the predictive value of insulin secretion or the disposition index on future development of PDM/DM because our OGTT data only include fasting and 120 minute stimulated insulin and glucose measures.

In summary, we discovered substantial disparity among static and dynamic IR indices in predicting future PDM/DM. Dynamic indices, $ISI_{0,120}$ and SiM, were consistently associated with future PDM/DM, diagnosed by either fasting glucose or postprandial glucose. But static indices, ISIgly_b and QUICKI, only predicted PDM/DM characterized by elevated fasting glucose. The superior dynamic IR indices reflect both hepatic and peripheral muscular IR, two equally important defects of IR underlying the development of PDM/DM. This study has important implications with regard to comprehensively understanding the pathogenesis of DM from an epidemiological perspective. Furthermore, given the longitudinal study design, this result also indicates that there possibly exist causal relationships from hepatic IR to PDM/DM characterized by high fasting glucose values and from peripheral IR to PDM/DM characterized by high stimulated glucose concentrations, respectively. Additionally, using dynamic indices to identify adults at risk of developing PDM/DM may increase the chance that interventions can be targeted more efficiently.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care. 1991; 14:173–94. [PubMed: 2044434]
2. Wagenmakers AJ. Insulin resistance in the offspring of parents with type 2 diabetes. PLoS Med. 2005; 2:e289. [PubMed: 16173834]
3. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979; 237:E214–23. [PubMed: 382871]

4. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin resistanceand resistance in vivo: advantages, limitations, and appropriate usage. Am J Physiol Endocrinol Metab. 2008; 294:E15–26. [PubMed: 17957034]
5. Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? Diabetes Care. 2007; 30:1544–8. [PubMed: 17384342]
6. Hanley AJ, Williams K, Gonzalez C, D'Agostino RB Jr, Wagenknecht LE, Stern MP, et al. Prediction of type 2 diabetes using simple measures of insulin resistance: combined results from the San Antonio Heart Study, the Mexico City Diabetes Study, and the Insulin Resistance Atherosclerosis Study. Diabetes. 2003; 52:463–9. [PubMed: 12540622]
7. Hanson RL, Pratley RE, Bogardus C, Narayan KM, Roumain JM, Imperatore G, et al. Evaluation of simple indices of insulin resistanceand insulin secretion for use in epidemiologic studies. Am J Epidemiol. 2000; 151:190–8. [PubMed: 10645822]
8. Wang B, Necheles J, Ouyang F, Ma W, Li Z, Liu X, et al. Monozygotic co-twin analyses of body composition measurements and serum lipids. Prev Med. 2007; 45:358–65. [PubMed: 17765960]
9. Wang G, Liu X, Christoffel KK, Zhang S, Wang B, Liu R, et al. Prediabetes is not all about obesity: association between plasma leptin and prediabetes in lean rural Chinese adults. Eur J Endocrinol. 2010; 163:243–9. [PubMed: 20511357]
10. Katz LD, Glickman MG, Rapoport S, Ferrannini E, DeFronzo RA. Splanchnic and peripheral disposal of oral glucose in man. Diabetes. 1983; 32:675–9. [PubMed: 6862113]
11. Belfiore F, Iannello S, Volpicelli G. Insulin resistanceindices calculated from basal and OGTT-induced insulin, glucose, and FFA levels. Mol Genet Metab. 1998; 63:134–41. [PubMed: 9562967]
12. Avignon A, Boegner C, Mariano-Goulart D, Colette C, Monnier L. Assessment of insulin resistancefrom plasma insulin and glucose in the fasting or post oral glucose-load state. Int J Obes Relat Metab Disord. 1999; 23:512–7. [PubMed: 10375055]
13. Gutt M, Davis CL, Spitzer SB, Llabre MM, Kumar M, Czarnecki EM, et al. Validation of the insulin resistanceindex (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract. 2000; 47:177–84. [PubMed: 10741566]
14. Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia. World Health Orgnization; http://www.who.int/diabetes/publications/Definition%20and%diagnosis%of%diabetes_new.pdf
15. Abdul-Ghani MA, Jenkinson CP, Richardson DK, Tripathy D, DeFronzo RA. Insulin secretion and action in subjects with impaired fasting glucose and impaired glucose tolerance: results from the Veterans Administration Genetic Epidemiology Study. Diabetes. 2006; 55:1430–5. [PubMed: 16644701]
16. Hanefeld M, Koehler C, Fuecker K, Henkel E, Schaper F, Temelkova-Kurktschiev T. Insulin secretion and insulin resistancepattern is different in isolated impaired glucose tolerance and impaired fasting glucose: the risk factor in Impaired Glucose Tolerance for Atherosclerosis and Diabetes study. Diabetes Care. 2003; 26:868–74. [PubMed: 12610051]
17. Abdul-Ghani MA, Tripathy D, DeFronzo RA. Contributions of beta-cell dysfunction and insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting glucose. Diabetes Care. 2006; 29:1130–9. [PubMed: 16644654]
18. Landau BR, Wahren J, Chandramouli V, Schumann WC, Ekberg K, Kalhan SC. Contributions of gluconeogenesis to glucose production in the fasted state. J Clin Invest. 1996; 98:378–85. [PubMed: 8755648]
19. DeFronzo RA, Ferrannini E. Regulation of hepatic glucose metabolism in humans. Diabetes Metab Rev. 1987; 3:415–59. [PubMed: 3552529]
20. Ferrannini E, Bjorkman O, Reichard GA Jr, Pilo A, Olsson M, Wahren J, et al. The disposal of an oral glucose load in healthy subjects. A quantitative study. Diabetes. 1985; 34:580–8. [PubMed: 3891471]
21. Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, et al. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care. 2007; 30:753–9. [PubMed: 17327355]

22. Bacha F, Lee S, Gungor N, Arslanian SA. From pre-diabetes to type 2 diabetes in obese youth: pathophysiological characteristics along the spectrum of glucose dysregulation. Diabetes Care. 2010; 33:2225–31. [PubMed: 20592052]

Abbreviations

PDM	pre-diabetes
DM	diabetes
OGTT	oral glucose tolerance test
IFG	isolated impaired fasting glucose
IGT	isolated impaired glucose tolerance
IFG&IGT	combined IFG and IGT
AROC	area under the receiver operating characteristic curve
QUICKI	quantitative insulin sensitivity index
ISIgly_b	Belfiore (basal) index
$ISI_{0,120}$	Gutt Insulin Sensitivity Index
SiM	Avignon's SiM
GEE	general estimation equation

Table 1

Sample characteristics (n=1143).

		Male (n=658)	Female (n=485)	P-value
		Mean (SD)		
Baseline	**Age(yr)**	37.2(10.7)	33.6(8.4)	<0.0001
	Weight(kg)	55.3(6.8)	50.0(6.7)	<0.0001
	Height(cm)	162(5.8)	152(5.5)	<0.0001
	BMI(kg/m^2)	21.2(2.3)	21.6(2.4)	0.001
	FPG(mmol/L)	4.6(0.6)	4.6(0.6)	0.27
	2HPG(mmol/L)	4.2(1.1)	4.8(1.0)	<0.0001
	logFPI(IU/ml)	1.7(0.7)	1.8(0.7)	0.005
	log2HPI(IU/ml)	2.5(0.8)	2.8(0.7)	<0.0001
Follow-up	**FPG(mmol/L)**	5.4(0.9)	5.5(0.9)	0.58
	2HPG(mmol/L)	5.6(2.2)	6.3(2.2)	<0.0001
		N(%)		
	Diabetes	17(3.3)	14(2.8)	
	Pre-diabetes*	72(10.9)	64(13.8)	0.52

* defined according to WHO criteria. BMI, body mass index. FPG, fasting plasma glucose. 2HPG, 2 hour postprandial glucose. FPI, fasting insulin. 2HPI, 2 hour postprandial insulin.

Table 2

Pearson's correlation coefficients between measures of insulin resistance indices at baseline and glucose level at follow-up with adjustment for gender.

Index(abbreviation)	Formula	Fasting glucose at follow-up	P-value	Postprandial glucose at follow-up	P-value
Static					
ISIgly_b	$2/[(I_0/mI_0 \times G_0/mG_0)+1]$	-0.12	<0.0001	-0.06	0.036
QUICKI	$1/(\log I_0+\log G_0)$	-0.10	0.0004	-0.06	0.056
Dynamic					
$ISI_{0,120}$	m/MPG/logMSI	-0.14	<0.0001	-0.12	<0.0001
SiM	$[(w \times Sib)+Si_{2h}]/2$	-0.16	<0.0001	-0.13	<0.0001

G_0, fasting glucose; G_2, 2-h glucose; I_0, fasting insulin; I_2, 2-h insulin; mG_0, mean fasting glucose; mI_0, mean fasting insulin; m =(75,000 mg + $(G_0 - G_2) \times 0.19 \times$Weight)/120 min(mg/min); MPG =$(G_0 + G_2)/2$(mg/dl); MSI=$(I_0+I_2)/2$(mU/L); w = mean Si2h/mean Sib, Sib=10^8/(FPI(mU/L)×FPG(mg/dl)×VD), Si2h =10^8/(2HPI (mU/L)×2-h glucose (mg/dl)×VD), where VD =150 ml/kg of body weight.

Table 3

AROC analyses of the predictive ability of insulin resistance indices to PDM/DM.

	AROC(95%CI)		
	PDM/DM By either FPG or 2HPG	**PDM/DM only by FPG**	**PDM/DM only by 2HPG**
Static			
ISIgly_b	0.54(0.49-0.59)	0.57(0.51-0.64)#	0.54(0.47-0.60)
QUICKI	0.54(0.49-0.59)	0.57(0.51-0.64)#	0.53(0.47-0.60)
Dynamic			
$ISI_{0,120}$	0.61(0.56-0.66)**	0.66(0.60-0.72)**	0.60(0.54-0.66)**
SiM	0.57(0.52-0.62)*	0.59(0.53-0.66)*	0.57(0.51-0.63)*

# P<0.05;

* P<0.01;

** P<0.001

Table 4

Risk of DM & PDM at follow-up predicted by baseline insulin resistance index.

Insulin Resistance Index			PDM/DM (n=173) by either FPG or 2HPG		PDM/DM (n=94) by FPG		PDM/DM (n=100) by 2HPG	
		Quartile	**N(%)**	**OR(95%CI)**	**N(%)**	**OR(95%CI)**	**N(%)**	**OR(95%CI)**
Static	ISIgly_b	2nd-4th	120(14.0)	reference	59(7.4)	reference	72(8.9)	reference
		1st	53(18.6)	1.4(1.0-2.1)	35(13.1)	1.9(1.2-3.0)*	28(10.8)	1.3(0.8-2.0)
	QUICKI	2nd-4th	120(14.0)	reference	59(7.1)	reference	72(8.9)	reference
		1st	53(18.6)	1.4(1.0-2.1)	35(13.1)	1.9(1.2-3.0)*	28(10.8)	1.3(0.8-2.0)
Dynamic	$ISI_{0,120}$	2nd-4th	106(12.4)	reference	53(6.6)	reference	61(7.5)	reference
		1st	67(23.5)	2.3(1.7-3.2)**	41(15.8)	2.8(1.8-4.2)**	39(15.2)	2.4(1.6-3.5)**
	SiM	2nd-4th	111(12.9)	reference	57(7.1)	reference	64(7.9)	reference
		1st	62(21.8)	1.8(1.3-2.6)**	37(14.2)	2.1(1.3-3.3)*	36(13.9)	1.9(1.2-2.9)*

*P<0.01;

**P<0.001.