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Predictability of 1-h postload plasma glucose concentration: A 10-year retrospective cohort study

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ABSTRACT

Aims/Introduction: Elevated 1-h postload plasma glucose concentration (1hPG) during oral glucose tolerance test has been linked to an increased risk of type 2 diabetes and a poorer cardiometabolic risk profile. The present study analyzed the predictability and cut-off point of 1hPG in predicting type 2 diabetes in normal glucose regulation (NGR) subjects, and evaluated the long-term prognosis of NGR subjects with elevated 1hPG in glucose metabolism, kidney function, metabolic states and atherosclerosis.

Materials and Methods: A total of 116 Han Chinese classified as NGR in 2002 at the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China, were investigated. Follow-up was carried out in 2012 to evaluate the progression of glucose metabolism, kidney function, metabolic syndrome and carotid atherosclerosis.

Results: The areas under receiver operating characteristic curves were higher for 1hPG than FPG or 2hPG (0.858 vs 0.806 vs 0.746). The cut-off value of 1hPG with the maximal sum of sensitivity and specificity in predicting type 2 diabetes in NGR subjects was 8.85 mmol/L. The accumulative incidence of type 2 diabetes in subjects with 1hPG ≥8.85 mmol/L was higher than those <8.85 mmol/L (46.2% vs 3.3%, $P = 0.000$; relative risk 13.846, 95% confidence interval 4.223–45.400). On follow up, the prevalence of metabolic syndrome and abnormal carotid intima-media thickness in the subjects with 1hPG ≥8.85 mmol/L tended to be higher compared with those <8.85 mmol/L.

Conclusions: 1hPG is a good predictor of type 2 diabetes in NGR subjects, and the best cut-off point is 8.85 mmol/L. Some tendency indicates that NGR subjects with 1hPG ≥8.85 mmol/L are more prone to metabolic syndrome and carotid atherosclerosis.

INTRODUCTION

The prevalence of type 2 diabetes keeps increasing[1]. Lifestyle modification and pharmacological intervention for high-risk populations can reduce the incidence of type 2 diabetes and its complications[2–5]. Identifying populations at high risk is important. Recent research has suggested that 1-h postload plasma glucose concentration (1hPG) during oral glucose tolerance test (OGTT) might be a strong predictor for type 2 diabetes in non-diabetic subjects, with a cut-off value of 8.6 mmol/L[6–9]. However, the predictive power of fasting glucose (FPG) and 1hPG it is still controversial, and the best cut-off value of 1hPG in predicting type 2 diabetes in normal glucose regulation (NGR) subjects has not been reported[6–9]. In addition, several cross-sectional studies reported that an elevated 1hPG is associated with chronic kidney disease (CKD) and atherosclerosis[10–12]. However, the long-term prognosis of patients with elevated 1hPG in CKD and atherosclerosis has not been reported. In contrast, a survey in a Chinese community assessed the cut-off values at 1hPG for impaired glucose regulation (IGR) and diabetes, and showed that the profiles of glucose and insulin in the subgroup with isolated 1-h hyperglycemia were very different from those seen in subjects with normal glucose tolerance or IGR[13], but the predictability of 1hPG for type 2 diabetes was not investigated. Therefore, in the present

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study, we followed up 116 NGR Han Chinese subjects for 10 years, aiming to investigate the long-term prognosis of NGR subjects with elevated 1hPG in glucose metabolism, kidney function, atherosclerosis and metabolic state, as well as to analyze the predictability and best cut-off point of 1hPG for type 2 diabetes.

MATERIALS AND METHODS

Study Population

In 2002, 309 Han Chinese participants, who were referred to the Department of Endocrinology, the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China, to have health examinations, were enrolled in a cross-sectional study assessing the single nucleotide polymorphism of calpain 10 and its relationship with insulin sensitivity[14]. Baseline data were collected including age, sex, family history of diabetes, bodyweight, height, body mass index (BMI), waist circumference, hip circumference, waist-to-hip ratio, systolic blood pressure and diastolic blood pressure. A 75-g OGTT was carried out, and the plasma glucose and serum insulin at fasting, and 1-h (serum insulin at 1 h during OGTT [1hINS]) and 2-h postload were measured. In 2012, we contacted all the NGR participants (150 altogether) by telephone, inviting them back for a free health examination on glucose metabolism and cardiovascular disease screening. The 116 responders among them, 36 men and 80 women, aged 55.0 years (ranging 51.6–61.2 years), free of self-reported cardiovascular diseases, cirrhosis, pregnancy, glucocorticoids administration or renal diseases at baseline, were re-recruited to participate in the present cohort study. They completed a follow-up examination, and had their diabetes, kidney function, carotid atherosclerosis and metabolic states outcomes determined. The study was approved by the institutional review board of the First Affiliated Hospital of Sun Yat-sen University. All participants gave their written informed consent before participation.

Definition of Variables and Outcomes of Glucose Metabolism

In 2012, a follow-up examination was carried out. All participants underwent a 75-g OGTT after a 12-h overnight fast. Plasma glucose was measured at 0, 30, 60 and 120 min. Glucose concentration was determined by the glucose oxidation method and serum insulin concentrations by the radioimmunoassay (RIA) technique using the kit by Beijing North Institute of Biological Technology (Beijing, China). Glycosylated hemoglobin A1c (HbA1c) was measured by high-performance liquid chromatography using an automated hemoglobin system (BIO-RAD Variant II; BIO-RAD, Hercules, CA, USA) and HemoglobinA1c Program Reorder peak Kit (BIO-RAD).

Type 2 diabetes was diagnosed according to the 2011 criteria by American Diabetes Association[15]. Glucose tolerance status was defined based on OGTT according to the World Health Organization 1999 criteria. FPG <6.1 mmol/L with 2 hPG <7.8 mmol/L was defined as NGR. In the present study, FPG <6.1 mmol/L with 2 hPG ranging from 7.8 to 11.1 mmol/L was defined as isolated IGT (I-IGT), whereas FPG ranging from 6.1 to 7.0 mmol/L with 2hPG from 7.8 to 11.1 mmol/L was defined as combined glucose intolerance (CGI).

Homeostasis model assessment of insulin resistance (HOMA-IR) and HOMA of β-cell function (HOMA-β) were calculated as: HOMA-IR = FPG × fasting plasma insulin (FINS)/22.5; HOMA-β = 20 × FINS × $(FPG - 3.5)^{-1}$. A variation of the Matsuda Index, which was calculated by using the mean of plasma glucose and insulin concentrations at 0 min, 1 h and 2 h during the OGTT in place of the mean of plasma glucose and insulin concentrations at 0, 30, 60, 90 and 120 min, was used to evaluate insulin sensitivity[16]. We referred to this index as the modified Matsuda Index (=10 000 × [FPG × FINS × mean OGTT $glucose_{(0–1h–2h)}$ × mean OGTT $insulin_{(0–1h–2h)}$]$^{1/2}$). The ratios of areas under the plasma insulin to glucose concentration curve (InsAuc/GluAuc) were calculated by the trapezoid rule: InsAuc1h/GluAuc1h = (FINS + 1hINS)/(FPG + 1hPG); InsAuc2h/GluAuc2h = (FINS + 1hINS + 1hINS + 2hINS)/(FPG + 1hPG + 1hPG + 2hPG). The ratios of the increment in serum insulin to the increment in plasma glucose were calculated as: $\triangle I_{0–1h}/\triangle G_{0–1h}$ = (1hINS − FINS)/(1hPG − FPG); $\triangle I_{0–2h}/\triangle G_{0-2h}$ = (2hINS − FINS)/(2hPG − FPG).

Definition of Variables and Outcomes of Kidney Function and Metabolic States

All participants underwent anthropometrical evaluation (weight, height, BMI, hip circumference and waist circumference), blood pressure readings, and laboratory measurements of lipid profile, uric acid (UA), serum creatinine (SCr), complete blood count and ratio of urinary microalbumin-to-creatinine concentration (U-mALB/Cr). Microalbuminuria was defined as U-mALB/Cr ranging from 30 to 300 mg/g. Estimated glomerular filtration rate (eGFR) was calculated with the CKD-EPI equation[17]: eGFR = 141 × min $(Scr/k, 1)^{\alpha}$ × max $(Scr/k, 1)^{-1.209}$ × 0.993^{Age} × 1.018 (if female) × 1.159, where k is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1. Renal dysfunction was defined as eGFR <90 mL/min per 1.73 m^2.

Metabolic syndrome (MS) was diagnosed according to the 2004 criteria by Chinese Diabetes Society (CDS)[18] (fulfilling three of the following leads to the diagnosis of MS: (i) BMI ≥25 kg/m^2; (ii) triglyceride (TG) >1.7 mmol/L; (iii) high density lipoprotein cholesterol [HDL-c] <0.9 mmol/L (if male), <1.0 mmol/L (if female); (iv) BP ≥140/90 mmHg; and (v) type 2 diabetes or FPG ≥6.1 mmol/L or 2hPG ≥7.8 mmol/L in 75-g OGTT).

Definition of Variables and Outcomes of Carotid Atherosclerosis

Intima-media thickness (IMT) of the common carotid artery was measured by high-resolution B-mode ultrasound with a Siemens-sequoia512 ultrasound system (Siemens, Berkeley, CA, USA) equipped with a 7.0–9.0-MHz transducer. Manual measurements were carried out in the plaque-free portions of

the 20-mm linear segment proximal to the carotid bulb. Plaque was defined as a clearly isolated focal thickening of the IMT as ≥1.3 mm. Abnormal carotid IMT was defined as ≥0.9 mm or plaque formation. For each participant, two measurements were carried out bilaterally, the values were averaged and presented as the mean of IMT of the common carotid artery.

Statistical Analysis

Continuous variables that followed normal distribution were presented as the means ± standard deviation, otherwise presented as the median (25th percentile, 75th percentile). Binary variables were expressed as the rate. The significance of the mean differences between continuous variables following normal distribution was tested with Student's *t*-test, while others were tested with the Mann–Whitney *U*-test. The χ^2-test was used to compare categorical variables, and the Mantel–Haenszel test was used to stratify potential confounders between groups. Assessment of the predictive discrimination of the various parameters was made using the receiver operating characteristic (ROC) curve. The area under the ROC curve was used to measure how well a continuous variable predicted the development

Table 1 | Univariate analysis of risk factors for type 2 diabetes

Variable	Non-diabetes	Diabetes	*P*
Sex (male/female)	31/70	5/10	1.000
Age (years)	55.0 (51.5–61.4)	55.5 (51.9–60.9)	0.866
Family history of type 2 diabetes (%)	24.8	46.7	0.118
Height (m)	1.60 ± 0.08	1.59 ± 0.08	0.728
Weight (kg)	60.10 ± 9.60	61.90 ± 9.56	0.500
BMI (kg/m^2)	23.48 ± 2.61	24.48 ± 3.09	0.180
Waist circumference (cm)	80.50 ± 8.21	82.75 ± 5.88	0.309
Hip circumference (cm)	94.02 ± 6.16	95.78 ± 6.43	0.308
Waist hip ratio	0.855 ± 0.062	0.864 ± 0.037	0.602
SBP (mmHg)	128.3 ± 18.5	126.3 ± 14.3	0.681
DBP (mmHg)	81.28 ± 10.73	80.27 ± 7.58	0.726
FPG (mmol/L)	4.97 ± 0.43	5.50 ± 0.41	0.000*
1hPG (mmol/L)	7.10 ± 1.80	9.95 ± 2.08	0.000*
2hPG (mmol/L)	5.63 ± 1.21	6.64 ± 0.71	0.000*
FINS (uIU/mL)	11.34 ± 5.73	10.31 ± 4.21	0.506
1hINS (uIU/mL)	69.51 ± 33.16	71.45 ± 34.26	0.834
2hINS (uIU/mL)	46.20 ± 25.97	56.62 ± 33.67	0.166
HOMA-IR	2.38 (1.72–2.94)	2.47 (1.70–3.27)	0.879
HOMA-β (%)	148.20 (110.95–193.40)	95.89 (75.63–136.77)	0.001*
Modified Matsuda Index	5.52 ± 2.36	4.68 ± 1.74	0.187
InsAuc1h/GluAuc1h	6.65 ± 2.55	5.25 ± 2.03	0.044*
InsAuc2h/GluAuc2h	7.92 ± 2.99	6.48 ± 2.55	0.079
$\Delta I_{0-1h}/\Delta G_{0-1h}$	25.24 (13.34–41.16)	13.16 (9.78–19.86)	0.022*
$\Delta I_{0-2h}/\Delta G_{0-2h}$	21.16 (–7.96–42.64)	20.46 (15.97–46.45)	0.303
Total cholesterol (mmol/L)	5.83 ± 1.07	5.79 ± 0.84	0.891
Triglyceride (mmol/L)	1.33 (1.02–1.84)	1.31 (1.01–2.17)	0.624
HDL c (mmol/L)	1.56 ± 0.41	1.53 ± 0.44	0.844
LDL c (mmol/L)	4.05 ± 1.22	4.06 ± 1.08	0.988
ApoA (mmol/L)	1.86 ± 0.29	1.90 ± 0.31	0.645
ApoB (mmol/L)	1.17 ± 0.34	1.20 ± 0.34	0.765
Metabolic syndrome (%)	7.9	13.3	0.616

*$P < 0.05$. Homeostasis model assessment of insulin resistance (HOMA-IR) = fasting plasma glucose (FPG) × fasting plasma insulin (FINS)/22.5. Homeostasis model assessment of β-cell function (HOMA-β) = 20 × FINS × (FPG − 3.5)$^{-1}$. Modified Matsuda Index = 10,000 × (FPG [mmol/L] × FINS [uIU/mL] × mean oral glucose tolerance test [OGTT] glucose$_{[0-1h-2h]}$ × mean OGTT insulin$_{[0-1h-2h]}$)$^{1/2}$. The ratio of areas under the plasma insulin to glucose concentration curve during the first hour of OGTT (InsAuc1h/GluAuc1h) = (FINS + 1-h plasma insulin [1hINS])/(FPG + 1-h postload plasma glucose [1hPG]). The ratio of areas under the plasma insulin to glucose concentration curve during the 2 h of OGTT (InsAuc2h/GluAuc2h) = (FINS + 1hINS + 1hINS + 2-h plasma insulin [2hINS])/(FPG + 1hPG + 1hPG + 2-h postload plasma glucose [2hPG]). The ratio of the increment in serum insulin to the increment in plasma glucose in the first hour during OGTT ($\Delta I_{0-1h}/\Delta G_{0-1h}$) = (1hINS − FINS)/(1hPG − FPG). The ratio of the increment in serum insulin to the increment in plasma glucose in the 2 h of OGTT ($\Delta I_{0-2h}/\Delta G_{0-2h}$) = (2hINS − FINS)/(2hPG − FPG). ApoA, apolipoprotein A; ApoB, apolipoprotein B; DBP, diastolic blood pressure; HDL c, high-density lipoprotein cholesterol; LDL c, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Table 2 | Contribution of baseline parameters to the risk for type 2 diabetes by a stepwise multivariate regression analysis

	B	Wald	*P*	OR	95% CI for OR
FPG	2.115	5.061	0.024	8.287	1.313–52.310
1hPG	0.733	10.062	0.002	2.081	1.323–3.273
InsAuc1h/GluAuc1h	–0.397	4.569	0.033	0.672	0.467–0.968

B, correlation coefficient; CI, confidence interval; OR, odds ratio; Wald, Wald statistics for logistic regression analysis. The ratio of areas under the plasma insulin to glucose concentration curve during the first hour of oral glucose tolerance test (InsAuc1h/GluAuc1h) = (fasting plasma insulin + 1-h plasma insulin)/(fasting plasma glucose [FPG] + 1-h postload plasma glucose [1hPG]).

of type 2 diabetes. Multivariate logistic regression was used to assess the contribution of baseline parameters to type 2 diabetes. All statistical analyses were carried out with SPSS 16.0 (Chicago, IL, USA) All *P*-values were based on two-sided tests, and the cut-off for statistical significance was 0.05.

RESULTS

Predictability of Baseline Parameters in Prediction of Type 2 Diabetes

Two participants were diagnosed as type 2 diabetes before the time of follow up, for whom only FPG and FINS were measured. A total of 15 participants had progressed to type 2 diabetes at follow up. The accumulative incidence of type 2 diabetes, CGI, and IFG or I-IGT were 12.9, 0.9 and 24.1%, respectively. In univariate analysis screening all the baseline parameters, type 2 diabetes was significantly associated with baseline FPG, 1hPG, 2hPG, HOMA-β, InsAuc1h/GluAuc1h and $\triangle I_{0-1h}/\triangle G_{0-1h}$ (Table 1). We carried out a stepwise multivariate regression analysis in a model including these six variables. The three variables that remained significantly associated with type 2 diabetes were FPG, 1hPG and InsAuc1h/GluAuc1h, among which 1hPG had the maximal Wald statistics, indicating that it was the most important and influential in this model (Table 2). 1hPG also had the greatest area under the ROC curve, and 8.85 mmol/L of 1hPG had the maximal Youden Index in predicting future type 2 diabetes, with 73.3% sensitivity and 86.0% specificity (Table 3, Figures 1 and 2).

Baseline Characteristics of the Study Groups Stratified by 1hPG

At baseline, 29.3% of the NGR participants had a 1hPG ≥8.6 mmol/L, and 22.4% had a 1hPG ≥8.85 mmol/L. Based on our finding of the cut-off value of 1hPG, we divided the participants into two groups: 90 individuals with 1hPG <8.85 mmol/L and 26 individuals with 1hPG ≥8.85 mmol/L. Table 4 shows the anthropometric, clinical and laboratory characteristics of the enrolled participants at baseline. Individuals with 1hPG ≥8.85 mmol/L had a worse metabolic and cardiovascular risk profile. They showed significantly higher FPG, 2hPG, 1-h plasma insulin (1hINS), 2-h plasma insulin (2hINS) and prevalence of MS, as well as lower HOMA-β, modified Matsuda Index, and $\Delta I_{0-1h}/\Delta G_{0-1h}$, as compared with individuals with 1hPG <8.85 mmol/L. They seemed to have higher BMI, total cholesterol, apolipoprotein B, triglyceride and the rate of type 2 diabetes family history, as compared with participants with 1hPG <8.85 mmol/L, although the differences were not statistically significant (Table 4). No significant differences between the two groups were observed with respect to age, sex, height, weight, waist circumference, hip circumference, waist-to-hip ratio, systolic blood pressure, diastolic blood pressure, HOMA-IR, FINS, high density lipoprotein cholesterol, low density lipoprotein cholesterol and apolipoprotein A.

Outcomes of Glucose Metabolism

At follow up, the conversion rates to type 2 diabetes, CGI, IFG or I-IGT were 46.2, 0.0 and 23.1% for participants with 1hPG ≥8.85 mmol/L, respectively. While those for participants with 1hPG <8.85 mmol/L were 3.3, 1.1 and 24.4%, respectively. The difference between the outcomes of glucose metabolism in the two groups was statistically significant ($P = 0.000$). The incidence of type 2 diabetes in participants with 1hPG

Table 3 | Predictability of baseline parameters in prediction of type 2 diabetes

	aROC	*P*	Cut-off value	Se	Sp	YI
FPG	0.806	0.000	5.35 mmol/L	0.733	0.812	0.545
1hPG	0.858	0.000	8.85 mmol/L	0.733	0.860	0.593
2hPG	0.746	0.002	5.30 mmol/L	1.000	0.406	0.406
HOMA-β	0.773	0.001	139.87%	0.933	0.564	0.497
InsAuc1h/GluAuc1h	0.686	0.020	5.43	0.800	0.667	0.467
$\triangle I_{0-1h}/\triangle G_{0-1h}$	0.684	0.022	19.93	0.800	0.646	0.446

2hPG, 2-h postload plasma glucose; aROC, area under the receiver operating characteristic curve; Se, sensitivity; Sp, specificity. Youden Index (YI) = sensitivity + specificity − 1. Homeostasis model assessment of β-cell function (HOMA-β) = 20 × fasting plasma insulin (FINS) × (fasting plasma glucose [FPG] − 3.5)$^{-1}$. The ratio of areas under the plasma insulin to glucose concentration curve during the first hour of oral glucose tolerance test (InsAuc1h/GluAuc1h) = (FINS + 1-h plasma insulin [1hINS])/(FPG + 1-h postload plasma glucose [1hPG]). The ratio of the increment in serum insulin to the increment in plasma glucose in the first hour during OGTT ($\triangle I_{0-1h}/\triangle G_{0-1h}$) = (1hINS − FINS)/(1hPG − FPG).

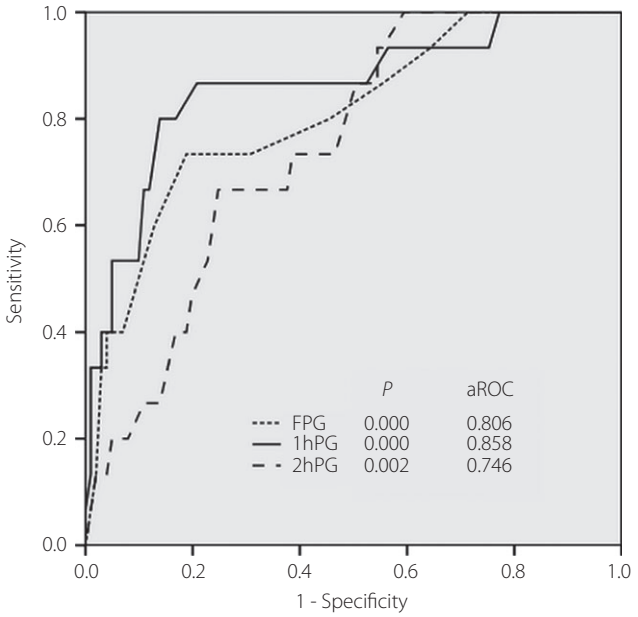

Figure 1 | Receiver operating characteristic curves of fasting plasma glucose (FPG), 1-h postload plasma glucose (1hPG) and 2-h postload plasma glucose (2hPG) in predicting type 2 diabetes. aROC, area under the receiver operating characteristic curve.

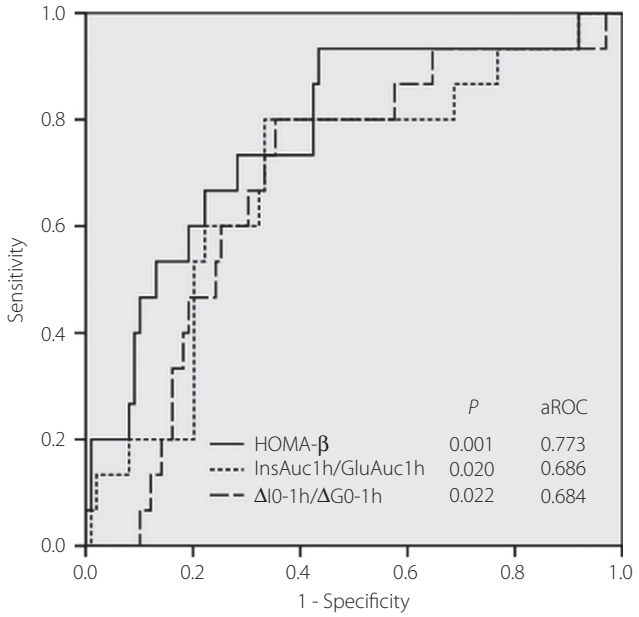

Figure 2 | Receiver operating characteristic curves of 2-h postload plasma glucose of homeostasis model assessment of β-cell function (HOMA-β), ratio of areas under the plasma insulin to glucose concentration curve during the first 1 h of oral glucose tolerance test (InsAuc1h/GluAuc1h) and $\Delta I_{0-1h}/\Delta G_{0-1h}$ in predicting type 2 diabetes. InsAuc1h/GluAuc1h = (fasting plasma insulin + serum insulin at 1-h during oral glucose tolerance test [1hINS])/(fasting plasma glucose + 1-h postload plasma glucose); $\Delta I_{0-1h}/\Delta G_{0-1h}$ = (1hINS – fasting plasma insulin)/(1-h postload plasma glucose – fasting plasma glucose). aROC, area under the receiver operating characteristic curve.

≥8.85 mmol/L was significantly higher than those <8.85 mmol/L ($P = 0.000$) with a relative risk of 13.846 (95% confidence interval 4.223–45.400; Table 5). This difference remained statistically significant after we stratified FPG and 2hPG with the Mantel–Haenszel χ^2-test ($P < 0.05$). At the time of follow up, participants with 1hPG ≥8.85 mmol/L compared with those <8.85 mmol/L showed higher HbA1c (6.22 ± 0.63 vs 5.79 ± 0.34%, $P = 0.003$) and lower HOMA-β (52.89 ± 39.42 vs 71.11 ± 35.00%, $P = 0.025$; Table 5).

Outcomes of Kidney Function, Metabolic States and Carotid Atherosclerosis

On follow up, there were no statistically significant differences in the prevalence of microalbuminuria and renal dysfunction between participants with 1hPG ≥8.85 mmol/L and those <8.85 mmol/L (Table 6). As for metabolic states, the prevalence of MS tended to be higher in participants with 1hPG ≥8.85 mmol/L than those <8.85 mmol/L, whereas the lipid profiles and serum uric acid levels were similar (Table 6). A total of 113 participants completed an ultrasound of the common carotid artery. The prevalence of abnormal carotid IMT tended to be higher in participants with 1hPG ≥8.85 mmol/L than those <8.85 mmol/L ($P = 0.050$), whereas there was no statistically significant difference in the prevalence of plaque formation between the two groups (Table 6).

DISCUSSION

Identification of individuals at high risk for type 2 diabetes and its complications is important for early intervention. IFG and IGT, categorized based on levels of FPG and 2hPG, are defined as prediabetes, presenting an increased risk for diabetes. However, longitudinal studies showed that a proportion of individuals who developed diabetes had NGR at baseline, showing that there is still a population of NGR subjects who are at risk for future diabetes, but are missed by intermittent screening of FPG and 2hPG[19]. Furthermore, several cross-sectional studies have showed that subjects with an elevated 1hPG have a poorer cardiometabolic risk profile, and elevated 1hPG is associated with an increased risk for CKD and cardiovascular diseases[10–12]. 1hPG is a predictor of type 2 diabetes, but the comparison of predictive power among 1hPG, FPG and 2hPG remains controversial[7,8,20,21], and the cut-off value of 1hPG in the prediction of diabetes in NGR subjects has not been reported. Here we carried out a 10-year cohort study, examining the long-term outcomes of NGR subjects with elevated 1hPG, with respect to the progression of glucose metabolism, kidney function, carotid atherosclerosis and metabolic syndrome. The predictability and cut-off value of 1hPG were also analyzed.

The present results showed that at baseline the prevalence of 1hPG elevation in NGR participants was 29.3% for ≥8.6 mmol/L and 22.4% for ≥8.85 mmol/L. As reported, the

Table 4 | Baseline characteristics of the participants stratified by 1-h postload plasma glucose

Variable	1hPG <8.85 mmol/L	1hPG ≥8.85 mmol/L	*P*
Sex (male/female)	28/62	8/18	0.974
Age (years)	55.0 (51.7–61.0)	55.3 (51.4–61.8)	0.997
Family history of type 2 diabetes (%)	24.4	38.5	0.156
Height (m)	1.60 ± 0.08	1.58 ± 0.08	0.455
Weight (kg)	60.11 ± 9.39	61.08 ± 10.30	0.652
BMI (kg/m^2)	23.44 ± 2.54	24.22 ± 3.12	0.193
Waist circumference (cm)	80.66 ± 7.84	81.24 ± 8.51	0.742
Hip circumference (cm)	94.18 ± 5.93	94.49 ± 7.15	0.822
Waist hip ratio	0.856 ± 0.058	0.859 ± 0.063	0.852
SBP (mmHg)	128.0 ± 18.4	128.4 ± 16.7	0.915
DBP (mmHg)	80.86 ± 10.89	82.15 ± 8.37	0.575
FPG (mmol/L)	4.96 ± 0.44	5.34 ± 0.43	0.000*
1hPG (mmol/L)	6.64 ± 1.41	10.32 ± 1.29	0.000*
2hPG (mmol/L)	5.58 ± 1.20	6.42 ± 1.02	0.002*
FINS (uIU/mL)	11.31 ± 5.89	10.85 ± 4.26	0.713
1hINS (uIU/mL)	64.71 ± 30.08	87.24 ± 37.76	0.002*
2hINS (uIU/mL)	44.68 ± 24.84	57.47 ± 32.58	0.035*
HOMA-IR	2.37 (1.70–2.93)	2.53 (1.73–3.00)	0.674
HOMA-β (%)	148.06 (111.41–196.35)	110.36 (77.27–158.45)	0.010*
Modified Matsuda Index	5.73 ± 2.38	4.31 ± 1.59	0.005*
InsAuc1h/GluAuc1h	6.54 ± 2.55	6.25 ± 2.47	0.607
InsAuc2h/GluAuc2h	7.81 ± 2.98	7.47 ± 2.96	0.610
$\Delta I_{0-1h}/\Delta G_{0-1h}$	29.71 (14.83–44.19)	13.91 (10.43–19.64)	0.000*
$\Delta I_{0-2h}/\Delta G_{0-2h}$	20.51 (–8.72–44.49)	21.58 (15.24–38.00)	0.693
Total cholesterol (mmol/L)	5.77 ± 1.05	6.02 ± 0.98	0.284
Triglyceride (mmol/L)	1.31 (1.00–1.80)	1.66 (1.06–2.21)	0.121
HDL-c (mmol/L)	1.56 ± 0.39	1.53 ± 0.46	0.769
LDL-c (mmol/L)	4.08 ± 1.23	3.98 ± 1.10	0.718
ApoA (mmol/L)	1.86 ± 0.29	1.87 ± 0.32	0.898
ApoB (mmol/L)	1.15 ± 0.35	1.24 ± 0.30	0.231
Metabolic syndrome (%)	5.6	19.2	0.044*

ApoA, apolipoprotein A; ApoB, apolipoprotein B; DBP, diastolic blood pressure; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure. *$P < 0.05$. Homeostasis model assessment of insulin resistance (HOMA-IR) = fasting plasma glucose (FPG) × fasting plasma insulin (FINS)/22.5. Homeostasis model assessment of β-cell function (HOMA-β) = 20 × FINS × (FPG − 3.5)$^{-1}$. Modified Matsuda Index = 10,000 × (FPG [mmol/L] × FINS [uIU/mL] × mean oral glucose tolerance test [OGTT] glucose$_{[0-1h-2h]}$ × mean OGTT insulin$_{[0-1h-2h]}$)$^{1/2}$. The ratio of areas under the plasma insulin to glucose concentration curve in the first hour during OGTT (InsAuc1h/GluAuc1h) = (FINS + 1-h plasma insulin [1hINS])/(FPG + 1-h postload plasma glucose [1hPG]). The ratio of the increment in serum insulin to the increment in plasma glucose in the 2 h of OGTT (InsAuc2h/GluAuc2h) = (FINS + 1hINS + 1hINS + 2-h plasma insulin [2hINS])/(FPG + 1hPG + 1hPG + 2-h postload plasma glucose [2hPG]). The ratio of the increment in serum insulin to the increment in plasma glucose in the first hour during OGTT ($\Delta I_{0-1h}/\Delta G_{0-1h}$) = (1hINS − FINS)/(1hPG − FPG). The ratio of the increment in serum insulin to the increment in plasma glucose in the 2 h of OGTT ($\Delta I_{0-2h}/\Delta G_{0-2h}$) = (2hINS − FINS)/(2hPG − FPG).

prevalence of 1hPG ≥8.6 mmol/L was 15% in Mexican Americans and Caucasians, and 8.3% in Latino Spanish[6,7,21,22], whereas 1hPG ≥7.8 mmol/L was found in 27.8% of NGR subjects in a community population in Shanghai, China[13]. We seemed to have a higher proportion of elevated 1hPG than that seen in Mexican Americans, Caucasians and Latino Spanish. In general, there was quite a proportion of Chinese NGR participants with 1hPG elevation as well as increased risk for diabetes, which should not be underestimated in terms of diabetes control.

Participants with 1hPG ≥8.85 mmol/L had lower HOMA-β and $\Delta I_{0-1h}/\Delta G_{0-1h}$ at baseline, indicating poorer β-cell function. The elevated postload plasma insulin levels in the 1-h ≥ 8.85 mmol/L group suggested more compensation is required for increased insulin resistance and postload hyperglycemia, thus a heavier burden on β-cells. Although glucose and insulin levels at 30 min were not measured at baseline, decreased ratio of $\Delta I_{0-1h}/\Delta G_{0-1h}$ in 1hPG elevated participants suggested poorer early insulin response. They also presented with lower modified Matsuda Index, indicating worse whole-body insulin

Table 5 | Outcomes of glucose metabolism based on stratification of 1-h postload plasma glucose

	1hPG <8.85 mmol/L	1hPG ≥8.85 mmol/L	*P*
Type 2 diabetes	3 (3.3%)	12 (46.2%)	0.000*
CGI	1 (1.1%)	0 (0.0%)	–
IFG or I-IGT	22 (24.4%)	6 (23.1%)	–
NGR	66 (71.1%)	8 (30.8%)	–
HbA1c (%)	5.79 ± 0.34	6.22 ± 0.63	0.003*
FINS (uIU/mL)	4.87 (3.72–6.86)	4.55 (2.93–6.32)	0.345
HOMA-IR	1.08 (0.83–1.56)	1.10 (0.76–1.58)	0.995
HOMA-β (%)	71.11 ± 35.00	52.89 ± 39.42	0.025*

1hPG, 1-h postload plasma glucose; CGI, combined glucose intolerance; HbA1c, glycosylated hemoglobin A1c, IFG, impaired fasting glucose; I-IGT, isolated impaired glucose tolerance; NGR, normal glucose regulation. *$P < 0.05$. Homeostasis model assessment of insulin resistance (HOMA-IR) = fasting plasma glucose (FPG) × fasting plasma insulin (FINS)/22.5. Homeostasis model assessment of β-cell function (HOMA-β) = $20 \times FINS \times (FPG - 3.5)^{-1}$.

Table 6 | Outcomes of kidney function, carotid atherosclerosis and metabolic states

	1hPG <8.85 mmol/L	1hPG ≥8.85 mmol/L	*P*
U-mALB/Cr (ug/mg)	7.0 (2.5–16.5)	10.0 (4.0–29.0)	0.236
Microalbuminuria, *n* (%)	11 (12.2)	6 (23.1)	0.208
Renal dysfunction, *n* (%)	35 (38.9)	13 (50.0)	0.311
Total cholesterol (mmol/L)	5.75 ± 1.00	5.70 ± 1.25	0.840
Triglyceride (mmol/L)	1.23 (0.90–1.81)	1.29 (1.01–1.79)	0.562
HDL-c (mmol/L)	1.52 ± 0.39	1.50 ± 0.39	0.872
LDL-c (mmol/L)	3.86 ± 1.40	3.73 ± 1.14	0.660
Uric acid (μmol/L)	288.62 ± 84.44	307.69 ± 79.67	0.307
Metabolic syndrome (%)	18.9	34.6	0.090
Abnormal carotid IMT, *n* (%)	56 (64.4)	22 (84.6)	0.050
Plaque formation, *n* (%)	43 (49.4)	15 (57.7)	0.459

ApoA, apolipoprotein A; ApoB, apolipoprotein B; HDL-c, high density lipoprotein cholesterol; IMT, intima-media thickness; LDL-c, low density lipoprotein cholesterol; UmALB/Cr, ratio of urinary microalbumin to creatinine concentration.

sensitivity. An increased prevalence of MS showed a poorer overall metabolic state. In accordance with previous studies[23,24], the NGR population with elevated 1hPG showed a poorer cardiometabolic risk profile.

1hPG is a good predictor for type 2 diabetes in NGR subjects, with the maximal area under the ROC curve, indicating a greater predictive power than FPG or 2hPG. This result is similar to the 7–8-year study in a non-diabetic population reported by Abdul-Ghani *et al.*[6], whereas it is different from the 3–5 year study in first-degree relatives of type 2 diabetes patients in the Isfahan diabetes prevention study (a combined population of NGR and prediabetes)[8]. The discordance might be due to the differences in races, sample sizes, inclusion criteria, sex ratio and duration of follow up. Furthermore, the present results showed that among the various baseline parameters, 1hPG contributed the most to the prediction model by multivariate logistic regression. In summary, for a Chinese NGR population, 1hPG is a stronger predictor of type 2 diabetes than FPG or 2hPG.

The increased risk for type 2 diabetes, CKD and cardiovascular diseases in a prediabetic population shown common origins of these diseases[25,26]. The ascending trend in the prevalence of abnormal carotid IMT in the elevated 1hPG group suggests 1hPG might be a risk factor for early atherosclerosis. The fact that the prevalence of diabetes was much higher in the elevated 1hPG group suggests that metabolic disturbances of diabetes could have affected the thickening of carotid IMT in this group. The NGR population with elevated 1hPG not only harbors a poorer cardiovascular risk profile, but also is related to poorer cardiovascular outcomes.

The present study had some limitations. The sample size was relatively small. As a retrospective study, the process of re-recruitment might have generated bias. OGTTs were carried out once, which could not rule out the influence of intraindividual variability. Also, the baseline data of renal function and carotid atherosclerosis was not available.

In conclusion, the present data suggest that NGR subjects with elevated 1hPG are at higher risk for type 2 diabetes. 1hPG is a good predictor for type 2 diabetes in NGR subjects, with a greater predictive power than FPG or 2hPG, and the cut-off point with maximal Youden Index is 8.85 mmol/L. As for long-term outcomes, NGR subjects with elevated 1hPG are more prone to metabolic disorders and atherosclerosis.

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DISCLOSURE

The authors declare no conflict of interest.

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