Research Article

A Prediction Model for Prediabetes Risk in Middle-Aged and Elderly Populations: A Prospective Cohort Study in China

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Background. To investigate indicators for prediabetes risk and construct a prediction model for prediabetes incidences in China.

Methods. In this study, 551 adults aged 40–70 years had normal glucose tolerance (NGT) and normal hemoglobin A1c (HbA1c) levels at baseline. Baseline data including demographic information, anthropometric measurements, and metabolic profile measurements were collected. The associations between possible indicators and prediabetes were assessed by the Cox proportional-hazards model. The predictive values were evaluated by the area under the receiver operating characteristic (ROC) curve (AUC).

Results. During an average of 3.35 years of follow-up, the incidence of prediabetes was found to be 19.96% (n = 110). In the univariate analyses, fasting plasma glucose (FPG), fasting serum insulin (FINS), 2h plasma glucose (2hPG), HbA1c, serum uric acid (SUA), waist circumference (WC), smoking, and family history of diabetes (FHD) were found to be significantly correlated with prediabetes. In the multivariable analyses, WC (hazard ratio (HR): 1.032; 95% confidence interval (CI): 1.010, 1.053; p < 0.003), FHD (HR: 1.824; 95% CI: 1.250, 2.661; p = 0.002), HbA1c (HR: 1.825; 95% CI: 1.227, 2.714; p = 0.003), and FPG (HR: 2.284; 95% CI: 1.556, 3.352; p < 0.001) were found to be independent risk factors for prediabetes. A model that encompassed WC, FHD, HbA1c, and FPG for predicting prediabetes exhibited the largest discriminative ability (AUC: 0.702).

Conclusions. WC, FHD, HbA1c, and FPG are independently correlated with the risk of prediabetes. Furthermore, the combination of these predictors enhances the predictive accuracy of prediabetes.

1. Introduction

Diabetes has evolved as a global health challenge. It is correlated with a high mortality rate, increased health risks, medical costs, and a poor quality of life. Prediabetes refers to the transition from normal glucose metabolism to diabetes, consisting of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) [1]. Prediabetic adults do not show any signs or symptoms of diabetes; therefore, many people are unaware that they are living with prediabetes [2]. Prediabetic individuals have an increased risk for diabetes, obesity, hypertension, dyslipidemia, cardiovascular disease, cancer, and dementia [3, 4]. Prediabetes prevention and control reduces the chances for progression to diabetes and its related complications.

In 2017, the World Health Organization documented that the global prevalence of diabetes and prediabetes has been on the rise [5]. Globally, China has the highest number of prediabetes patients, with a prevalence of 35.2% in 2017. This corresponds to approximately 357 million people [6]. A Chinese study involving adults with IGT reported that the cumulative incidence of type 2 diabetes in 6 years was 67.7% [7]. Therefore, it is important to identify indicators that efficiently predict prediabetes development. This will help monitor patients and improve intervention.

Diabetes pathogenesis involves interactions between genes and the environment. Factors influencing prediabetes include age [8, 9], educational attainment [9], marital status [9], hypertension [10], dyslipidemia [11], gestational diabetes, body mass index (BMI) [9, 12], WC [12], FHD [13],
diet patterns [14], and 1-hour plasma glucose levels [15]. In
Japan, a prognostic model based on six variables was built to
predict the incidences of type 2 diabetes mellitus and pre-
diabetes in a healthy population [16]. The AUC of the
predictive model was found to be 0.87. Moreover, a model
for screening prediabetes in Indonesian adults
(AUC = 0.623), which includes age, sex, education level,
FHD, smoking, physical activity, BMI, and hypertension, has
been developed and verified [17]. However, a prediction
model for predicting prediabetes incidences in China has not
been constructed. Therefore, we aimed at investigating the
potential indicators and to construct a prediction model for
prediabetes incidence among middle-aged and elderly
populations in urban areas of Hangzhou, China.

2. Methods

2.1. Study Participants. Participants enrolled in this cohort
study were from the Caihe community of Jianggan Dis-
trict, Hangzhou. Participants, aged between 40 and 70
years, were recruited by community workers. Recruitment
was done between January and March 2010. Follow-up
done was in 2011, 2013, and 2015. The exclusion criteria
were as follows: (i) those using glucocorticoids; (ii) those
with cirrhosis and ascites; (iii) hyperthyroidism or hy-
pothyroidism; (iv) cancer; (v) severe disabilities or mental
diseases; (vi) pregnant and lactating women; (vii) par-
ticipants with diabetes or prediabetes at baseline; (viii)
those with incomplete information; (ix) lost at follow-up;
and (x) new-onset diabetes before the diagnosis of pre-
diabetes at follow-up. For all participants, there was at
least one visit between 2011 and 2015. The study was
approved by the ethics committee of Sir Run Run Shaw
Hospital. Informed consent was provided by all
participants.

2.2. Demographic Characteristics. Age, gender, education
levels, nature of occupation, cigarette smoking habits, al-
cohol drinking habits, dietary patterns, regular exercise, and
FHD data were obtained by a questionnaire. Participants
were grouped based on cigarette smoking habits, that is,
smoker, exsmoker, and nonsmoker. Moreover, they were
categorized based on alcohol drinking habits, that is,
drinker, exdrinker, and nondrinker. Education levels were
categorized as middle school or above and below middle
school. The nature of occupation before retirement was
defined as manual work, physical and mental work, and
mental work. Dietary patterns were divided into main meat
dishes, balanced meat and vegetables, and main vegetable
dishes. The FHD was defined as the presence of diabetes
among first-degree relatives. Regular exercise was more than
1 day per week.

2.3. Assessment of Anthropometric Measurements and Met-
abolic Profiles. The measurement of WC, blood pressure,
BMI, FPG, FINS, SUA, high-density lipoprotein cholesterol
(HDL-C), triglyceride (TG) levels, and 2hPG levels was
based on the previous article [18].

2.4. Definition. The definition of hypertension was systolic
blood pressure (SBP) ≥140 mmHg and/or diastolic blood
pressure (DBP) ≥90 mmHg and/or diagnosed as hypertension
by a physician previously. The definition of diabetes was FPG
≥7.0 mmol/L, 2hPG ≥11.1 mmol/L, or previously diagnosed
as diabetes. The definition of prediabetes was 7.0 mmol/
L > FPG ≥ 6.1 mmol/L, 11.1 mmol/L > 2hPG ≥ 7.8 mmol/L,
or previously diagnosed as diabetes.

2.5. Statistical Analysis. All analyses were performed with R
3.5.0 and SPSS 26.0. Continuous variables were shown as
means ± standard deviations, medians (interquartile ranges),
or frequencies and percentages. Continuous variables with a
skewed distribution were transformed by natural logarithm
transformation before analysis. Comparison between 2
groups was conducted by independent-samples t-test for
continuous variables, while χ² tests were used for categorical
variables. The multivariable Cox model was performed to
estimate the correlations between indicators and prediabetes
incidences. Clinically relevant baseline variables or var-
iables with p < 0.2 upon univariate analysis were entered
into the multivariate analysis. Variables were entered into
the multivariate Cox proportional-hazards model one by
one. They were kept in the final models, which were added
to this model, changing the matched hazard ratio by at
least 10 percent or if the p value by itself made sense. The
variance inflation factor of the variables included in the
model was examined to address collinearity. No evidence
of collinearity was noted in the model, given the variance
inflation factor of < 5. The ROC was applied to compare
the predictive accuracy of various models. Differences
between AUC were determined using DeLong’s test.
Additionally, integrated discrimination improvement
(IDI), net reclassification index (NRI), and Akaike’s in-
formation criterion (AIC) were calculated to evaluate the
predictive values of different models. p ≤ 0.05 was con-
sidered statistically significant.

3. Results

3.1. Basic Characteristics of the Study Participants. A total of
1,030 participants were initially enrolled from January to
March 2010. Among them, 223 had prediabetes or type 2
diabetes at baseline, 243 were lost at follow-up, while 5
participants had incomplete data. Eight participants were
excluded because they were diagnosed as type 2 diabetes at
follow-up. Finally, 551 eligible participants were enrolled
(Figure 1). During an average of 3.35 years of follow-up, 110
of the 551 participants without dysglycemia at baseline
developed prediabetes (incidence: 19.96%). Demographic,
clinical, and biological characteristics of 551 participants are
shown in Table 1. Average age at baseline was 53.23 ± 6.62
years in the NGT group and 54.42 ± 7.02 years in the pre-
diabetes group. Participants with prediabetes outcomes
exhibited significantly elevated WC, BMI, FPG, 2hPG,
HbA1c, FINS, and SUA levels as well as significantly sup-
pressed HDL-C level at baseline. Moreover, at baseline,
proportion of male, prevalence of hypertension, smoking,
and FHD were significantly higher in participants with prediabetes. At baseline, there were no significant differences in age, TG, alcohol drinking, dietary patterns, nature of occupation, education level, and regular exercise.

3.2. Associations between Possible Indicators and the Risk of Prediabetes. In the univariate analyses (Additional file 1: Table S1), FPG, FINS, 2hPG, HbA1c, SUA, WC, smoking, and FHD were found to be significantly correlated with prediabetes. The FPG was the strongest predictor for prediabetes. In the multivariate model, 16 variables (age, gender, hypertension, smoking, drinking, FHD, regular exercise, WC, BMI, FPG, FINS, 2hPG, HbA1c, SUA, HDL-C, and TG) were selected into the model for screening. The final prognostic models are shown in Table 2. Given the relationship between WC and glucose metabolism, WC was set as the base model (model 1), which was easy to be clinically obtained. Model 2 additionally included FHD. The variables in model 2 plus HbA1c were selected for model 3. Model 4 additionally included FPG. Multivariate Cox proportional-hazard analyses showed that WC (HR: 1.032; 95% CI: 1.010–1.053; \( p < 0.003 \)), FHD (HR: 1.824; 95% CI: 1.250, 2.661; \( p = 0.002 \)), HbA1c (HR: 1.825; 95% CI: 1.227, 2.714; \( p = 0.003 \)), and FPG (HR: 2.284; 95% CI: 1.556, 3.352; \( p < 0.001 \)) were independent risk factors of prediabetes.

3.3. Predictive Values of FPG, HbA1c, WC, and FHD for Prediabetes. The predictive accuracy of the resultant models for prediabetes was evaluated by ROC curve analysis (Figure 2). The established independent risk factors for prediabetes were used to construct the predictive model. The AUC was 0.637 when WC was used alone (model 1). The addition of FHD (model 2) in model 1 did not significantly increase the AUC (model 2 versus model 1: DeLong’s test, \( p = 0.7901 \)). However, a significant increase in AUC was observed when HbA1c and FPG were further added (model 3 versus model 2: DeLong’s test, \( p = 0.0205 \); model 4 versus model 3: DeLong’s test, \( p = 0.0013 \)), with AUC eventually increasing to 0.702 (model 4). Discriminative abilities of the resultant models were confirmed using the NRI, IDI, and AIC measures (Table 3). Model 4 exhibited the smallest AIC measure and significantly enhanced risk reclassification and discrimination (NRI, 30.4%; 95% CI: 0–38.9%; IDI, 10.4%; 95% CI: 1.7–21.5%) when compared with model 1.

4. Discussion

In this study, we found that FPG, HbA1c, WC, and FHD are independently associated with the development of prediabetes among middle-aged and elderly adults in China. Moreover, the potential of the developed prognostic model for screening the individual risk of developing prediabetes was high.

People with visceral obesity are more likely to develop prediabetes [19]. Glucose utilization in the peripheral tissues and the liver is affected by changes in tissue proportions and increase of free fatty acids. This causes gluconeogenesis, which results in insulin resistance, thereby increasing the risk of prediabetes [20]. WC is a simple and commonly used marker for visceral obesity and is correlated with a higher risk of prediabetes among Chinese and Iranian adults [12]. Our study confirmed this finding. The WC was independently correlated with a 1.032-fold (95% CI: 1.010–1.053)
increased risk of prediabetes. Despite the power of WC for predicting prediabetes, its predictive value was not strong enough as an independent predictor in the clinical setup. Other risk factors should be considered to improve its ability as a predictive tool for prediabetes.

FHD is a predictor for prediabetes development. A multicenter study found that FHD was significantly correlated with prediabetes development [21]. This relationship remained significant when adjusted for gender, age, and BMI. Moreover, FHD in a first-degree relative was associated with IFG among children and adolescents [22]. In this study, FHD was independently correlated with a 1.824-fold (95% CI: 1.250–2.661) increased risk of prediabetes. The results are in line with the reported familial clustering risk and may be related to genetics and family environment [23].

Besides WC and FHD, FPG was correlated with a higher risk for prediabetes in our study. FPG was independently correlated with a 2.284-fold (95% CI: 1.556–3.352) increased risk of prediabetes. This outcome has been confirmed in other studies. An increase in FPG within the normal range is

### Table 1: Basic characteristics of study participants categorized by glucose metabolism.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NGT (n = 441)</th>
<th>Prediabetes (n = 110)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.23 ± 6.62</td>
<td>54.42 ± 7.02</td>
<td>0.093</td>
</tr>
<tr>
<td>Gender, men (%)</td>
<td>149 (33.80)</td>
<td>52 (47.30)</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.01 ± 2.67</td>
<td>23.77 ± 2.73</td>
<td>0.007</td>
</tr>
<tr>
<td>WC, cm</td>
<td>76.47 ± 8.40</td>
<td>80.56 ± 8.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FPG, mmol/L</td>
<td>4.70 ± 0.46</td>
<td>4.98 ± 0.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FINS, μU/mL</td>
<td>5.73 ± 4.31</td>
<td>7.54 ± 6.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2hPG, mmol/L</td>
<td>5.03 ± 1.14</td>
<td>5.52 ± 1.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c, mmol/mol</td>
<td>36.32 ± 4.57</td>
<td>38.45 ± 4.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.47 ± 0.42</td>
<td>5.67 ± 0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SUA, μmol/L</td>
<td>272.77 ± 84.21</td>
<td>299.83 ± 81.56</td>
<td>0.003</td>
</tr>
</tbody>
</table>
| **Table 2: Multivariable Cox proportional-hazards regression models for predicting prediabetes.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 HR (95% CI)</th>
<th>p value</th>
<th>Model 2 HR (95% CI)</th>
<th>p value</th>
<th>Model 3 HR (95% CI)</th>
<th>p value</th>
<th>Model 4 HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC</td>
<td>1.039 (1.018, 1.061)</td>
<td>&lt;0.001</td>
<td>1.039 (1.018, 1.061)</td>
<td>&lt;0.001</td>
<td>1.039 (1.018, 1.061)</td>
<td>&lt;0.001</td>
<td>1.032 (1.010, 1.053)</td>
<td>0.003</td>
</tr>
<tr>
<td>FHD</td>
<td>—</td>
<td>—</td>
<td>1.924 (1.320, 2.805)</td>
<td>0.001</td>
<td>2.028 (1.382, 2.976)</td>
<td>&lt;0.001</td>
<td>2.284 (1.556, 3.352)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.844 (1.262, 2.693)</td>
<td>0.0002</td>
<td>1.824 (1.250, 2.661)</td>
<td>0.002</td>
</tr>
<tr>
<td>FPG</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.250 (1.227, 2.714)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Model 1: incorporating WC; model 2: variables in model 1 and FHD; model 3: variables in model 2 and HbA1c; model 4: variables in model 3 and FPG.

Values are means ± standard deviations, n (%), or medians (interquartile ranges). *Natural logarithm transformed before analysis. BMI: body mass index; WC: waist circumference; FPG: fasting plasma glucose; FINS: fasting serum insulin; HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein cholesterol; NGT: normal glucose tolerance; SUA: serum uric acid; TG: triglycerides; 2hPG: 2h plasma glucose.
correlated with increased incidences of IGT and IFG [24]. Elevated FPG (within the normal range) is a predictor for prediabetes and diabetes development during youth, middle, and old ages [25]. These studies confirm that an increase in FPG is potentially useful in identifying healthy people who are at risk of developing prediabetes. Furthermore, we found that HbA1c is correlated with a higher risk for prediabetes. This is the first work to be performed in China to determine whether HbA1c is beneficial in risk prediction of prediabetes. Interestingly, HbA1c was independently correlated with a 1.825-fold (95% CI: 1.227–2.714) increased risk of prediabetes.

Most of the domestic studies have used a single index to predict prediabetes. In a 2020 study, it was shown that the...
triglyceride-glucose index (TyG index) was considered as a potential predictor for identifying high-risk individuals with prediabetes. The AUC for the TyG index in predicting prediabetes was found to be 0.60 [11]. The Chinese visceral adiposity index (CVAI) is considered as a better indicator for predicting prediabetes than WC in Chinese adults. The AUC for the CVAI was found to be 0.64 in women and 0.57 in men [12]. Visceral adiposity index (VAI), waist-height ratio (WHtR), and WC were considered as independent predictors for prediabetes in women over 40 years. The AUC of VAI, WHtR, and WC for predicting prediabetes was 0.625, 0.602, and 0.598, respectively [26]. All the aforementioned predictors were not independently strong enough to predict prediabetes in the clinical setup (AUC < 0.70). A combination of different predictors enhances the predictive accuracy for prediabetes. In this study, multivariate Cox proportional-hazard analyses revealed that WC, FHD, HbA1c, and FPG were independent risk factors of prediabetes. A combination of FPG, HbA1c, WC, and FHD was input in model 4 to predict prediabetes. ROC curve analysis was finally conducted to evaluate the predictive ability of the model for prediabetes (AUC = 0.702; Figure 2). AIC, NRI, and IDI were used to compare the prediction models. They exhibited better predictive values of FPG, HbA1c, WC, and FHD for prediabetes (Table 3). This is the first study to construct a multivariate prediction model, which included demographic characteristics, anthropometric measurements, and metabolic profiles for Chinese adults.

The functions of islets gradually decline with age, including weakened insulin action, leading to lipid and glucose metabolism disorder. Prediabetes incidences are correlated with age [27]. Gender has also been reported to be correlated with prediabetes incidences. For instance, the prevalence of prediabetes was significantly higher in males than in females [28]. However, it was reported that gender and age were not correlated with prediabetes in another study [29]. This is in line with our study, potentially due to the sample size and differences in the districts of participants. This warrants further investigations.

This work has some limitations. First, the study population is from a single community in southern China, with limited representation. Therefore, the true effect of this model should be further investigated and verified in different populations. Second, correlations stratified by age and gender were unexplored because of sample size limitations. Third, although many people were lost to follow-up, no significant statistical differences were noted in basic characteristics for the 243 lost and 551 follow-up participants.

Therefore, the 551 followed up participants may validly represent the entire study cohort. Despite its limitations, the model can still be used, given that few models have been developed to predict prediabetes in the Chinese population.

5. Conclusions
FPG, HbA1c, WC, and FHD are independently correlated with the increased risk of prediabetes. A combination of these predictors enhances the predictive accuracy for prediabetes. We developed a multivariate prognostic model to predict the risk of prediabetes development. This may help in identifying high-risk populations and to develop preventive strategies.

Data Availability
The data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval
The authors certify that they complied with the ethical guidelines for authorship and publishing. This study was approved by the ethics committee of Sir Run Run Shaw Hospital.

Consent
All the patients signed an informed consent form to participate.

Conflicts of Interest
The authors declare that they have no conflicts of interest.

Acknowledgments
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Supplementary Materials
Table S1: univariate Cox proportional-hazards regression models for predicting prediabetes. (Supplementary Materials)
References


