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Association between insulin resistance and multiple chronic diseases: a cross-sectional study from CHARLS

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Abstract

Background Chronic disease is a global public health problem. This study aimed to explore the association between insulin resistance (IR)-related indices and various chronic diseases, and to evaluate the predictive capacity of IR-related indices for these diseases.

Methods The data used in this study came from CHARLS. Binary logistic regression analysis and RCS were used to analyze the relationship between IR-related indices, including TyG, TyG-BMI, TyG-WHtR, METS-IR and eGDR, with nine chronic diseases. Subgroup analysis was performed to test the stability of the results. Finally, the predictive power of IR-related indices for chronic diseases was tested by ROC curve.

Results A total of 8,177 participants were included in this study. The study found that elevated prevalence of multiple chronic diseases is positively associated with increases in TyG, TyG-BMI, TyG-WHtR, and METS-IR, and negatively associated with eGDR. ROC analysis revealed that IR-related indices had the best accuracy in predicting dyslipidemia compared to other diseases, with TyG being the best predictor.

Conclusions IR-related indices were positively associated with the prevalence of multiple chronic diseases. The burden of chronic diseases can be reduced by improving IR in middle-aged and older people.

Keywords Insulin resistance, Chronic disease, CHARLS

Introduction

The occurrence of chronic diseases is a major public health challenge shared globally [1]. Old age is a persistent and important risk factor for chronic diseases [2]. China is one of the countries in the world with the highest degree of aging, the largest number of aging population and the fastest rate of aging [3]. According to the 2022 China Health Statistical Yearbook, the number of people with chronic diseases in China will exceed 500 million by 2024 [4]. It has been shown that insulin resistance (IR) is an important influence on the development of chronic diseases in middle-aged and elderly people [5]. Assessing and targeting the level of IR in the population can help promote early prevention of chronic diseases.

The diminished physiologic role of insulin in the body is defined as IR [6]. The high insulin-normal glucose clamp technique is the gold standard for assessing IR, but it is expensive and invasive, making it of low utility in clinical trials [7]. Therefore, a number of simple indices that do not rely on serum insulin levels have been used as alternatives for assessing IR, including triglyceride glucose

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index (TyG), triglyceride glucose-body mass index (TyG-BMI), triglyceride glucose-waist-to-height ratio (TyG-WHtR), metabolic score of IR (METS-IR) and estimated glucose disposal rate (eGDR) [8–11]. Compared to the high insulin-normal glucose clamp technique, the above indices are less costly and more time efficient, making them more suitable for clinical studies. Previous studies have shown that in addition to diabetes, IR is associated with a variety of chronic diseases such as cardiovascular disease [12], kidney disease [13], hyperuricemia [14], arthritis [15], and others. However, most of these studies have only explored the relationship between a single IR-related indicator and a single disease. Meanwhile, relevant studies based on Chinese middle-aged and elderly people are still rare.

To more comprehensively assess the relationship between IR and chronic diseases, we conducted a cross-sectional study based on the China Health and Retirement Longitudinal Study (CHARLS). The aim of this study is to understand the association between IR and chronic diseases among Chinese middle-aged and elderly people, so as to prevent, control and intervene in the occurrence of various chronic diseases in a more targeted manner.

Methods

Study population

The data used in this study were downloaded from CHARLS, which is a nationally representative survey of people over 45 years of age in China [16]. The study was approved by the ethics committee of Peking University (IRB00001052–11015). CHARLS uses the 2011 survey as a baseline, with follow-up visits every 2 to 3 years thereafter (2013, 2015, 2018, and 2020) to follow up and assess participants' health status, lifestyle habits, socioeconomic status, and other aspects of their lives. In 2013 and 2015, CHARLS collected and tested blood samples from participants. The study will use CHARLS 2015 data. Based on our research needs, we processed the data as follows.

Firstly, we excluded 11,218 participants with incomplete data [fasting plasma glucose (FPG), body mass index (BMI), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), glycated hemoglobin A (HbA1c), waist circumference, and hypertension] used to calculate IR-related indices. Secondly, 1,023 participants who lacked diagnostic indicators for chronic diseases [hypertension, hepatopathy, heart disease, digestive disease, arthritis, asthma, dyslipidemia, hyperuricemia, chronic kidney disease (CKD)] and 33 participants with missing covariates (gender, age, residence, education, region, marital status, smoking status, alcohol status, disability, diabetes, BMI) were also excluded. In addition, participants who were younger than 45 years old, had cancer, or suffered from mental illness or memory disorders were not included in the study. Ultimately, a total of 8,177 participants who met the criteria were enrolled in this study (Fig. 1).

Calculation of IR-related indices

In this study, a total of five indices were selected as proxies for IR. Calculate the eGDR using the following equation: eGDR is equal to 21.158– [0.09 × waist circumference (cm)] – [3.407 × HT]– [0.551 × HbA1c (%)], where HT = hypertension (yes = 1/no = 0). Other IR-related indices were calculated according to the following formula.

$$TyG = \frac{ln\left[TG(\,mg/dl) \times\ FPG(mg/dl\,)\right]}{2}$$

$$TyG - BMI = TyG \times \frac{body\ mass}{\text{height}^2}$$

$$TyG - WHtR = TyG \times \frac{waist\ circumference}{\text{Height}}$$

$$MEST - IR = ln\frac{[2 \times\ FPG(mg/dl) + TG(mg/dl\,)] \times\ BMI}{ln[HDL - c(mg/dl0]}$$

Definition of chronic diseases

Nine chronic diseases were included as variables in this study. Hypertension was diagnosed based on the following conditions: (1) the mean blood pressure value of three measurements ≥ 130 mmHg for systolic blood pressure or ≥ 80 mmHg for diastolic blood pressure (2), self-reported history of hypertension, and (3) self-reported intake of anti-hypertensive drugs [17]. Dyslipidemia was defined as having total cholesterol ≥ 200 mg/dl, TG ≥ 150 mg/dl, HDL-c < 40 mg/dl in males and < 50 mg/dl in females, low-density lipoprotein cholesterol ≥ 130 mg/dl, or self-reported history of dyslipidemia [18]. Hyperuricemia was delineated as a serum uric acid ≥ 7.0 mg/dl in males or ≥ 6.0 mg/dl in females [14]. CKD was defined as estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m^2 or a self-reported history of CKD. We used Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) to determine eGFR [13]. Diagnoses of other chronic diseases (hepatopathy, heart disease, digestive disease, arthritis, and asthma) were derived from self-reported disease histories.

Assessment of covariates

For demographic variables, gender (male and female), age (categorized as 40–59, and ≥ 60), residence (city and country), education levels (below primary school, primary school, middle school, and high school and above), region (northeastern China, eastern China, western China, and central China) and marital status (no

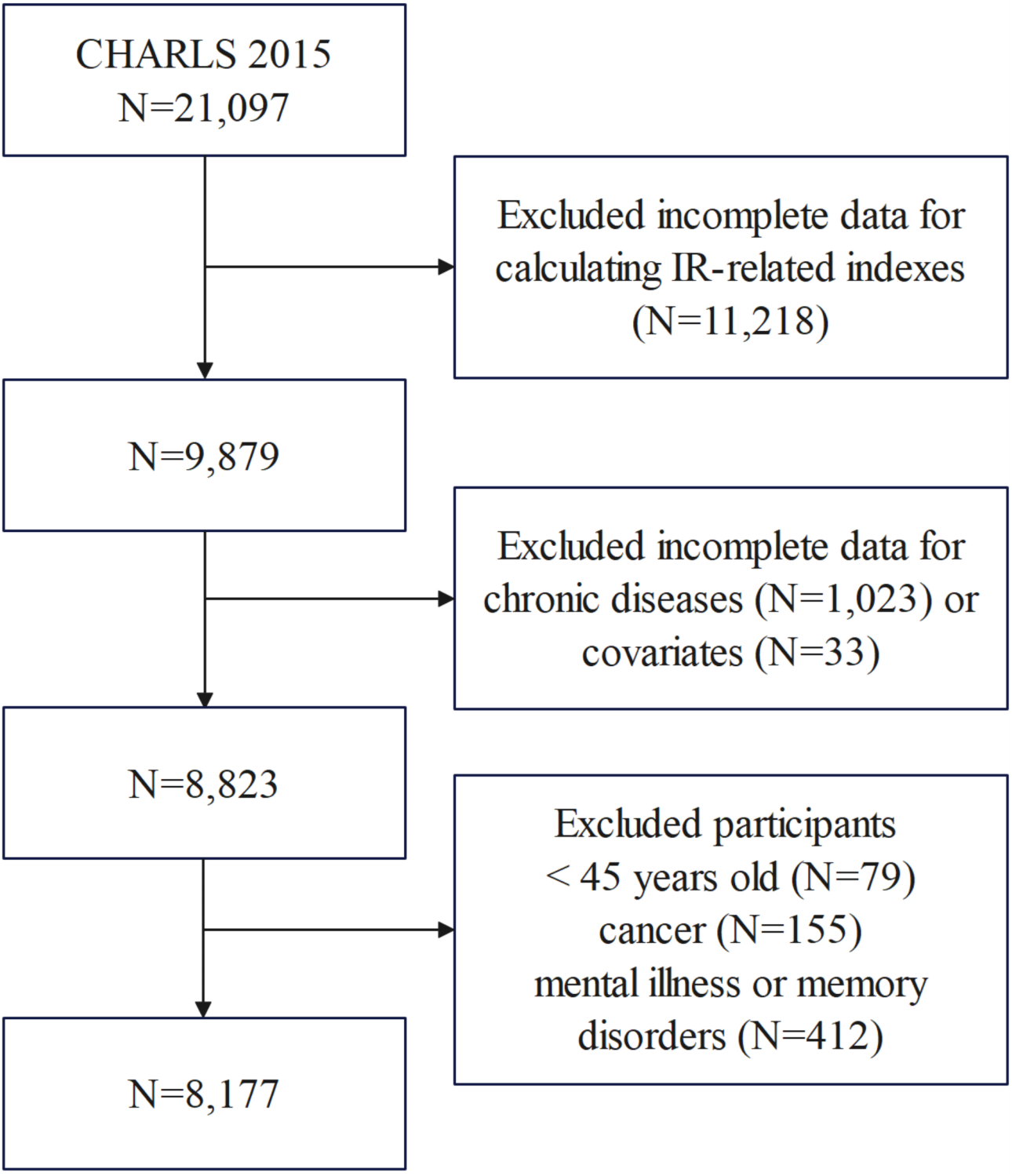

Fig. 1 Flowchart of the sample selection from CHARLS 2015. *CHARLS* China Health and Retirement Longitudinal Study, *IR* insulin resistance

partner, married or living with a partner, and separation) were obtained from the interview by standardized questionnaires. According to the question "Do you currently smoke?" question, smoking status was categorized as either current smoker or current nonsmoker, and based on the question "Have you ever smoked before?" Participants who were not current smokers were categorized as having a smoking history and never having smoked. Alcohol status is categorized as "never drank", "drinking history", and "drink now" based on the same

methodology. The determination of whether a participant is disabled is made by professionally trained CHARLS investigators. Diabetes was defined by FBG ≥ 126 mg/dl, HbA1c ≥ 6.5%, self-reported diagnosis, or use of oral hypoglycemic medication or insulin [19]. BMI was categorized into four groups: thin (BMI < 18.5 kg/m^2), normal (18.5 kg/m^2 ≤ BMI < 25 kg/m^2), overweight (25 kg/m^2 ≤ BMI < 30 kg/m^2), and obesity (BMI ≥ 30 kg/m^2) [20].

Statistical analysis

Categorical data were expressed as counts and percentages, and statistically analyzed using the chi-square test or Fisher's exact probability test (with theoretical numbers < 10). Normally distributed continuous data were expressed as mean and standard deviation, and t-tests for two independent samples were used to compare differences between groups. Continuous data with skewed distributions were expressed as M (Q1, Q3) in quadratic scores, and between-group comparisons were made using the two-sample independent rank-sum test.

We used three logistic regression models to examine the association of IR-related indicators with chronic diseases. Model 1 was unadjusted; model 2 was adjusted for gender, age, residence, education level, region, and marital status; and model 3 was further adjusted for smoking status, drinking status, disability status, diabetes, and BMI. Next, the dose–response relationship (linear or nonlinear) between IR-related indices and chronic diseases was investigated by the restricted cubic spline (RCS) model. Models fitted by RCS were adjusted for the same covariates as in model 3 performed.

Subgroup analysis was conducted to assess whether there was a potential effect of gender, age, residence, education level, region, marital status, smoking status, drinking status, disability status, diabetes, and BMI.

The diagnostic value of IR-related indices was analyzed using the receiver operating characteristic (ROC) curve, and the area under the curve (AUC) was calculated to quantify its predictive ability for chronic diseases.

Data processing and analysis were performed using STATA 18.0, R version 4.3.0 and Zstats software (www.medsta.cn/software). Differences between groups were considered statistically significant at $P < 0.05$.

Results

Baseline characteristics of the participants

Of the 8,177 participants analyzed in this study, 53.25% were female, 56.72% were over 60 years of age, and 64.31% of the population lived in rural areas. The highest prevalence of chronic diseases is dyslipidemia [$n = 4,847$ (59.28%)], followed by hypertension [$n = 4,298$ (52.56%)]. For any of chronic diseases, participants with a history of smoking or drinking had a higher risk of developing the disease. Meanwhile, in a between-group comparison carried out according to the presence of hypertension, heart disease, dyslipidemia or hyperuricemia, all IR-related indices of the patients changed significantly ($p < 0.05$). All baseline characteristics are listed in Supplementary Table.

Associations of IR-related indices with chronic diseases

The associations between TyG and chronic diseases were shown in Table 1. The results showed that TyG was only associated with heart disease, dyslipidemia, and hyperuricemia ($p < 0.05$). After adjusting for covariates, the association between TyG and heart disease was no longer significant, while asthma showed a negative association with TyG.

The associations between TyG-BMI and chronic diseases were shown in Table 2. There was a positive association between TyG-BMI and hypertension, heart disease, dyslipidemia, and hyperuricemia ($p < 0.05$). When adjusted to model 2, the association between TyG-BMI and hyperuricemia was no longer significant. When

Table 1 Associations of triglyceride glucose index (TyG) with the risk of chronic diseases

Variables	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Hypertension	1.01 (0.91 ~ 1.12)	0.847	0.94 (0.82 ~ 1.07)	0.349	0.89 (0.78 ~ 1.03)	0.112
Hepatopathy	0.99 (0.86 ~ 1.15)	0.944	0.93 (0.78 ~ 1.12)	0.456	0.87 (0.72 ~ 1.06)	0.169
Heart disease	1.33 (1.22 ~ 1.45)	**< 0.001**	1.04 (0.93 ~ 1.17)	0.481	1.03 (0.91 ~ 1.16)	0.682
Digestive disease	0.93 (0.86 ~ 1.00)	0.055	1.04 (0.94 ~ 1.14)	0.433	0.99 (0.90 ~ 1.10)	0.858
Arthritis	0.97 (0.90 ~ 1.04)	0.395	0.91 (0.83 ~ 1.00)	0.058	0.91 (0.83 ~ 1.01)	0.070
Asthma	0.87 (0.75 ~ 1.02)	0.078	0.74 (0.60 ~ 0.92)	**0.006**	0.69 (0.56 ~ 0.86)	**0.001**
Dyslipidemia	13.12 (11.56 ~ 14.90)	**< 0.001**	11.62 (10.07 ~ 13.40)	**< 0.001**	12.12 (10.47 ~ 14.03)	**< 0.001**
Hyperuricemia	2.04 (1.84 ~ 2.27)	**< 0.001**	1.49 (1.28 ~ 1.72)	**< 0.001**	1.61 (1.37 ~ 1.88)	**< 0.001**
CKD	1.01 (0.91 ~ 1.12)	0.847	0.94 (0.82 ~ 1.07)	0.349	0.89 (0.78 ~ 1.03)	0.112

OR: Odds Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjust: Gender, Age, Residence, Education, Region, Marital

Model 3: Adjust: Gender, Age, Residence, Education, Region, Marital, Smoking, Alcohol, Disability, Diabetes, BMI

Table 2 Associations of triglyceride glucose-body mass index (TyG-BMI) with the risk of chronic diseases

Variables	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Hypertension	1.01 (1.01 ~ 1.01)	**< 0.001**	1.04 (1.03 ~ 1.06)	**< 0.001**	1.05 (1.03 ~ 1.06)	**< 0.001**
Hepatopathy	1.00 (1.00 ~ 1.00)	0.862	1.00 (0.99 ~ 1.01)	0.542	1.00 (0.99 ~ 1.01)	0.845
Heart disease	1.01 (1.01 ~ 1.01)	**< 0.001**	0.99 (0.99 ~ 0.99)	**0.020**	1.00 (0.99 ~ 1.00)	0.210
Digestive disease	1.00 (1.00 ~ 1.00)	0.316	1.00 (1.00 ~ 1.01)	0.339	1.00 (1.00 ~ 1.01)	0.105
Arthritis	1.00 (1.00 ~ 1.00)	0.709	1.00 (0.99 ~ 1.00)	0.593	1.00 (1.00 ~ 1.00)	0.916
Asthma	1.00 (1.00 ~ 1.00)	0.281	1.00 (0.99 ~ 1.01)	0.978	1.00 (0.99 ~ 1.01)	0.435
Dyslipidemia	1.01 (1.01 ~ 1.02)	**< 0.001**	0.99 (0.99 ~ 0.99)	**< 0.001**	0.99 (0.99 ~ 0.99)	**0.001**
Hyperuricemia	1.01 (1.01 ~ 1.01)	**0.007**	1.00 (0.99 ~ 1.00)	0.123	1.00 (0.99 ~ 1.00)	0.142
CKD	1.00 (1.00 ~ 1.00)	0.976	0.99 (0.99 ~ 0.99)	**0.031**	1.00 (0.99 ~ 1.00)	0.090

OR: Odds Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjust: Gender, Age, Residence, Education, Region, Marital

Model 3: Adjust: Gender, Age, Residence, Education, Region, Marital, Smoking, Alcohol, Disability, Diabetes, BMI

Table 3 Associations of triglyceride glucose-waist-to-height ratio (TyG-WHtR) with the risk of chronic diseases

Variables	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Hypertension	1.58 (1.50 ~ 1.67)	**< 0.001**	0.01 (0.01 ~ 0.01)	**< 0.001**	0.01 (0.01 ~ 0.01)	**< 0.001**
Hepatopathy	1.00 (0.91 ~ 1.10)	0.983	0.99 (0.84 ~ 1.17)	0.919	0.98 (0.82 ~ 1.18)	0.864
Heart disease	1.30 (1.23 ~ 1.38)	**< 0.001**	0.90 (0.80 ~ 1.01)	0.073	0.85 (0.75 ~ 0.95)	**0.006**
Digestive disease	0.91 (0.86 ~ 0.95)	**< 0.001**	0.93 (0.86 ~ 1.01)	0.103	0.96 (0.88 ~ 1.05)	0.395
Arthritis	1.02 (0.98 ~ 1.07)	0.291	1.06 (0.97 ~ 1.15)	0.199	1.03 (0.94 ~ 1.13)	0.489
Asthma	1.03 (0.93 ~ 1.13)	0.597	1.46 (1.15 ~ 1.85)	**0.002**	1.56 (1.21 ~ 2.00)	**< 0.001**
Dyslipidemia	2.66 (2.49 ~ 2.84)	**< 0.001**	1.03 (0.93 ~ 1.13)	0.567	1.03 (0.93 ~ 1.14)	0.605
Hyperuricemia	1.49 (1.38 ~ 1.60)	**< 0.001**	1.44 (1.19 ~ 1.74)	**< 0.001**	1.31 (1.08 ~ 1.58)	**0.006**
CKD	1.03 (0.96 ~ 1.10)	0.384	1.05 (0.94 ~ 1.19)	0.384	1.09 (0.96 ~ 1.23)	0.193

OR: Odds Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjust: Gender, Age, Residence, Education, Region, Marital

Model 3: Adjust: Gender, Age, Residence, Education, Region, Marital, Smoking, Alcohol, Disability, Diabetes, BMI

adjusted to model 3, the association between TyG-BMI and heart disease was no longer significant.

The associations between TyG-WHtR and chronic diseases were shown in Table 3. There was a positive association between TyG-WHtR and hypertension, heart disease, dyslipidemia, hyperuricemia, and a negative association with digestive disease ($p < 0.05$). After adjusting for covariates, the relationship between TyG-WHtR and hypertension shifted to a negative association, and a positive association with hyperuricemia remained. Asthma and TyG-WHtR were not associated in model 1, but were positively associated in models 2 and 3 ($p < 0.05$).

The associations between METS-IR and chronic diseases were shown in Table 4. METS-IR was positively associated with hypertension and dyslipidemia in all three models ($p < 0.05$). Positive associations between METS-IR and heart disease (model 1, model 2), hyperuricemia (model 1), and CKD (model 2) were found only in some models ($p < 0.05$).

The associations between eGDR and chronic diseases were shown in Table 5. Of the five IR-related indices, eGDR associated with the greatest number of chronic diseases (hypertension, heart disease, digestive disease, asthma, dyslipidemia, hyperuricemia, and CKD). In all three models, eGDR was negatively associated with four chronic diseases (hypertension, heart disease, dyslipidemia, and hyperuricemia) and positively associated with digestive disease ($p < 0.05$).

RCS analysis investigating the relationship between IR-related indices and chronic diseases

Since there were many undifferentiated results in model 3 ($P > 0.05$), we used RCS to model and illustrate the nonlinear associations between IR-related indices and chronic diseases in a flexible manner. By analyzing these nondifferential results in model 3, we found that six diseases had nonlinear relationships with IR-related indices. The risk of hypertension (Fig. 2-A) rises when the TyG index is greater than 8.58. When the TyG-BMI index is greater than 204.66, the risk of heart disease (Fig. 2-B),

Table 4 Associations of metabolic score of insulin resistance (METS-IR) with the risk of chronic diseases

Variables	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Hypertension	1.03 (1.03 ~ 1.04)	**< 0.001**	0.88 (0.81 ~ 0.96)	**0.003**	0.87 (0.79 ~ 0.96)	**0.006**
Hepatopathy	1.00 (1.00 ~ 1.00)	0.782	1.02 (0.97 ~ 1.06)	0.522	1.00 (0.96 ~ 1.05)	0.871
Heart disease	1.01 (1.01 ~ 1.01)	**< 0.001**	1.04 (1.01 ~ 1.07)	**0.006**	1.02 (0.99 ~ 1.06)	0.113
Digestive disease	1.00 (0.99 ~ 1.00)	0.195	0.99 (0.96 ~ 1.01)	0.380	0.98 (0.96 ~ 1.01)	0.124
Arthritis	1.00 (1.00 ~ 1.00)	0.925	1.01 (0.98 ~ 1.03)	0.593	1.00 (0.97 ~ 1.02)	0.897
Asthma	1.00 (0.99 ~ 1.00)	0.325	0.99 (0.94 ~ 1.03)	0.550	0.97 (0.92 ~ 1.02)	0.182
Dyslipidemia	1.08 (1.07 ~ 1.09)	**< 0.001**	1.05 (1.02 ~ 1.08)	**< 0.001**	1.05 (1.02 ~ 1.08)	**< 0.001**
Hyperuricemia	1.01 (1.01 ~ 1.01)	**0.004**	1.02 (0.98 ~ 1.05)	0.325	1.02 (0.98 ~ 1.05)	0.398
CKD	1.00 (1.00 ~ 1.00)	0.885	1.04 (1.01 ~ 1.07)	**0.033**	1.03 (1.00 ~ 1.06)	0.093

OR: Odds Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjust: Gender, Age, Residence, Education, Region, Marital

Model 3: Adjust: Gender, Age, Residence, Education, Region, Marital, Smoking, Alcohol, Disability, Diabetes, BMI

Table 5 Associations of estimated glucose disposal rate (eGDR) with the risk of chronic diseases

Variables	Model 1		Model 2		Model 3	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Hypertension	0.15 (0.14 ~ 0.16)	**< 0.001**	0.03 (0.02 ~ 0.03)	**< 0.001**	0.02 (0.01 ~ 0.03)	**< 0.001**
Hepatopathy	0.97 (0.93 ~ 1.01)	0.093	0.95 (0.91 ~ 1.00)	0.050	0.98 (0.93 ~ 1.03)	0.430
Heart disease	0.83 (0.81 ~ 0.85)	**< 0.001**	0.83 (0.80 ~ 0.86)	**< 0.001**	0.86 (0.83 ~ 0.89)	**< 0.001**
Digestive disease	1.07 (1.05 ~ 1.09)	**< 0.001**	1.05 (1.02 ~ 1.07)	**< 0.001**	1.06 (1.03 ~ 1.09)	**< 0.001**
Arthritis	0.99 (0.97 ~ 1.01)	0.458	0.98 (0.96 ~ 1.01)	0.127	0.99 (0.97 ~ 1.02)	0.610
Asthma	0.93 (0.90 ~ 0.97)	**< 0.001**	0.97 (0.92 ~ 1.02)	0.208	0.98 (0.93 ~ 1.03)	0.439
Dyslipidemia	0.80 (0.79 ~ 0.82)	**< 0.001**	0.94 (0.91 ~ 0.97)	**< 0.001**	0.93 (0.90 ~ 0.96)	**< 0.001**
Hyperuricemia	0.81 (0.79 ~ 0.84)	**< 0.001**	0.91 (0.87 ~ 0.94)	**< 0.001**	0.92 (0.88 ~ 0.96)	**< 0.001**
CKD	0.96 (0.93 ~ 0.99)	**0.003**	0.96 (0.92 ~ 0.99)	**0.014**	0.97 (0.93 ~ 1.00)	0.087

OR: Odds Ratio, CI: Confidence Interval

Model 1: Crude

Model 2: Adjust: Gender, Age, Residence, Education, Region, Marital

Model 3: Adjust: Gender, Age, Residence, Education, Region, Marital, Smoking, Alcohol, Disability, Diabetes, BMI

digestive disease (Fig. 2-C), and hyperuricemia (Fig. 2-D) is elevated. At a TyG-WHtR index greater than 4.71, there is an increased risk of digestive disease (Fig. 2-E) and dyslipidemia (Fig. 2-F). When the METS-IR index was greater than 34.98, participants had a higher risk of heart disease (Fig. 2-G), digestive disease (Fig. 2-H), and hyperuricemia (Fig. 2-I).

Subgroup analysis

Subgroup analyses were conducted for IR-related indices and chronic diseases for which linear or nonlinear associations existed. The results showed that the association of IR-related indices and the prevalence of chronic diseases remained consistent in most subgroups (P for interactions > 0.05). However, subgroup analysis associated with TyG showed that former smokers and people with diabetes had a lower risk of asthma, and people of normal weight or overweight had a higher risk of hyperuricemia (Fig. 3). Subgroup analyses of TyG-BMI associations showed that normal or overweight people were more likely to have hypertension, those with less than elementary or more than high school education, no current alcohol use, and overweight were more likely to have heart disease, those who lived in urban areas and were of normal weight were more likely to have digestive disorders, those who were not obese were more likely to have dyslipidemia, and those who were overweight were more likely to have hyperuricemia (Fig. 4). TyG-WHtR showed stronger positive associations with hypertension, dyslipidemia, and hyperuricemia in normal-weight and overweight populations, with heart disease in never-smokers and current smokers, and showed negative associations with asthma in smoking cessation and diabetic populations (Fig. 5). When METS-IR indexe was higher than 34.98, high school education and above, a history of alcohol consumption, and being overweight were high risk factors for heart disease, living in city and being of normal weight were high risk factors for digestive disease, and having a middle school education and being overweight were high risk factors for hyperuricemia (Fig. 6). In non-diabetic patients, eGDR showed a stronger negative association with hyperuricemia (Fig. 7).

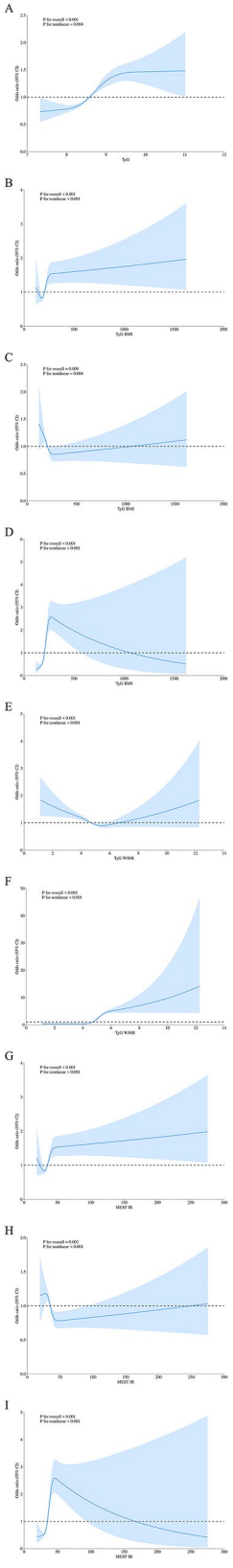

Fig. 2 Results of RCS analysis. Associations between IR-related indices with the risk of hypertension (**A**), heart disease (**B**, **G**), digestive disease (**C**, **E**, **H**), hyperuricemia (**D**, **I**) and dyslipidemia (**F**) were evaluated by restricted cubic spline after adjustment for the covariables in model 3. The solid blue lines correspond to the central estimates, and the light blue regions indicate the 95% confidence intervals. The dashed lines parallel to the X-axis indicate that odd ratio = 1

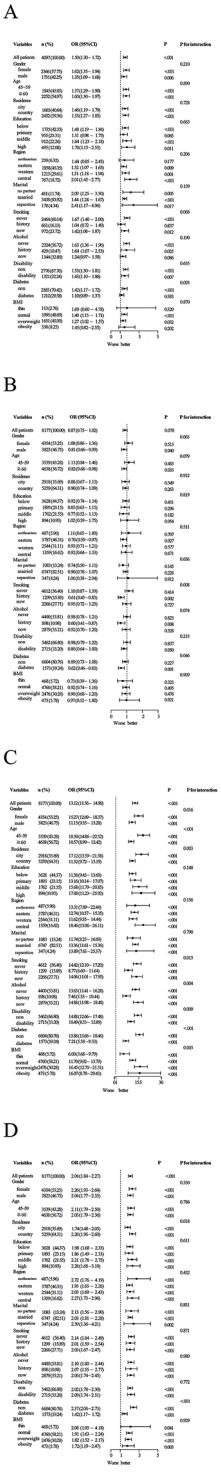

Fig. 3 Forest plot of TyG. Forest plot of triglyceride glucose index (TyG) association with the risk of **A** hypertension, **B** asthma, **C** dyslipidemia and **D** hyperuricemia

Diagnostic efficacy of IR-related indices for chronic diseases

The ROC curve assesses diagnostic efficacy using the magnitude of the AUC: the closer the AUC is to 1, the higher the diagnostic value (Fig. 8). Most of the AUCs were between 0.5 and 0.7, indicating that the diagnostic value of these models is poor. However, the diagnosis of

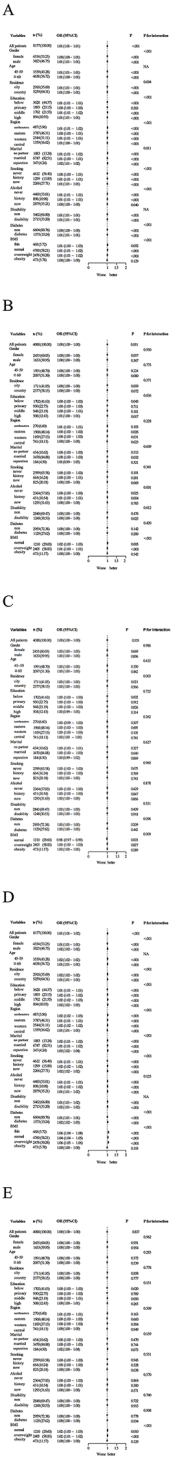

Fig. 4 Forest plot of TyG-BMI. Forest plot of triglyceride glucose-body mass index (TyG-BMI) association with the risk of **A** hypertension, **B** heart disease, **C** digestive disease, **D** dyslipidemia and **E** hyperuricemia

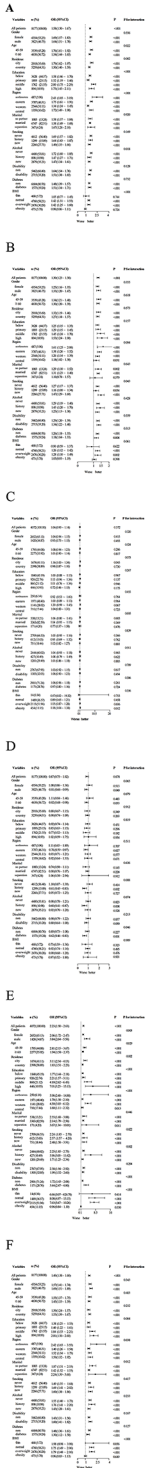

Fig. 5 Forest plot of TyG-WHtR. Forest plot of triglyceride glucose-waist-to-height ratio (TyG-WHtR) association with the risk of **A** hypertension, **B** heart disease, **C** digestive disease, **D** asthma, **E** dyslipidemia and **F** hyperuricemia

dyslipidemia by IR-related indices has some accuracy. TyG (AUC:0.8089, 95%CI:0.7997 ~ 0.818) is the best predictor of dyslipidemia, followed by TyG-WHtR (AUC:0.7355, 95%CI:0.7247 ~ 0.7463). Since hypertension is the variable used to calculate the eGDR, the very high diagnostic efficacy of the eGDR for hypertension is not meaningful.

Discussion

This cross-sectional study of 8,177 individuals revealed associations between five IR-related indices and the occurrence of nine chronic diseases. The findings support that elevated prevalence of multiple chronic diseases is positively associated with increases in TyG (hypertension, asthma, dyslipidemia, hyperuricemia), TyG-BMI

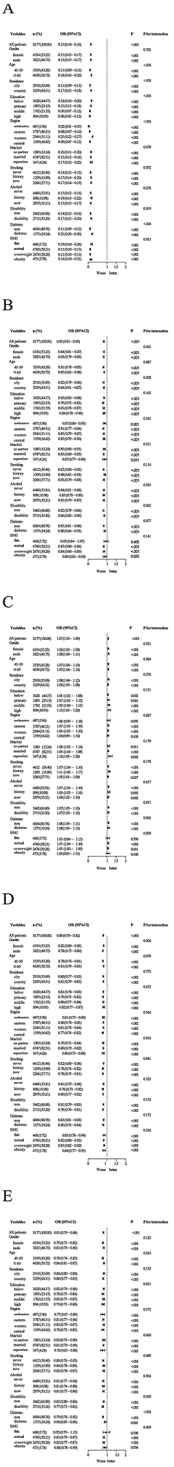

Fig. 6 Forest plot of METS-IR. Forest plot of metabolic score of IR (METS-IR) association with the risk of **A** hypertension, **B** heart disease, **C** digestive disease, **D** dyslipidemia and **E** hyperuricemia

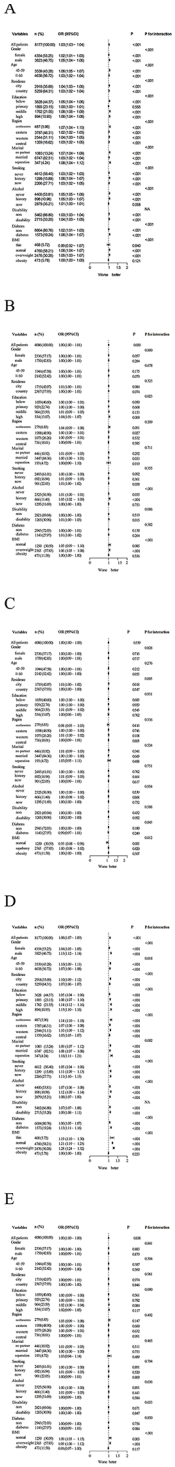

Fig. 7 Forest plot of eGDR. Forest plot of estimated glucose disposal rate (eGDR) association with the risk of **A** hypertension, **B** heart disease, **C** digestive disease, **D** dyslipidemia and **E** hyperuricemia

(hypertension, heart disease, digestive disease, dyslipidemia, hyperuricemia), TyG-WHtR (hypertension, heart disease, digestive disease, asthma, dyslipidemia, hyperuricemia), and METS-IR (hypertension, heart disease, digestive disease, dyslipidemia, hyperuricemia), and negatively associated with eGDR (hypertension, heart disease, digestive disease, dyslipidemia, hyperuricemia). Subgroup studies demonstrated that different groups with elevated IR-related indices had distinct associations with the risk of multiple chronic diseases. ROC analysis revealed that IR-related indices had the best accuracy in predicting dyslipidemia compared to other diseases, with TyG being the best predictor.

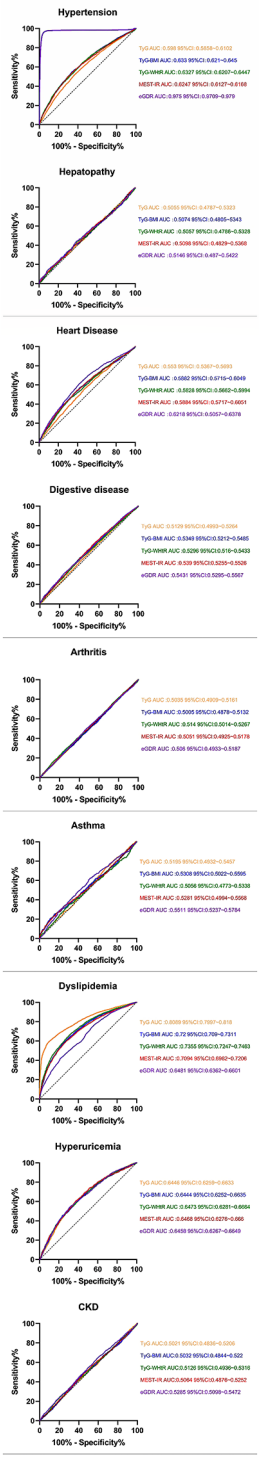

Fig. 8 Diagnostic efficacy of metabolic score of IR-related indices for chronic diseases

Our results showed that the three metabolic diseases (hypertension, dyslipidemia, hyperuricemia) associated with all IR-related indices used in the study. The association between IR and risk of hypertension has been widely discussed in recent years. Observational and genetic studies support that IR increases the risk of hypertension [21, 22]. The effect of IR on the development of hypertension is currently the subject of two main speculations. One possible mechanism is that IR-induced hyperinsulinism activates the renin-angiotensin-aldosterone system, which induces the onset of renal sodium retention, ultimately leading to increased blood pressure [23]. Another possible pathway is IR stimulation of sympathetic nervous system activity, which induces epinephrine and norepinephrine secretion, leading to increased cardiac output and peripheral vascular resistance through vascular smooth muscle cell hypertrophy and endothelial dysfunction [24]. A close relationship between IR and elevated TG levels and reduced HDL-c levels has been demonstrated, which involves several early steps in insulin signaling to lipolysis and adipogenesis in adipocytes [25]. Meanwhile, higher rates of lipolysis in adipocytes contribute to higher levels of free fatty acids and subsequent hepatic fat accumulation, which in turn induces the progression of IR [26]. The significant association between IR and hyperuricemia has been supported by evidence in Asian populations [27, 28]. IR-induced disruption of glycolysis is one of the mechanisms by which hyperuricemia occurs [29]. In addition, IR affects the renal mechanism of uric acid functioning and promotes the reabsorption of uric acid [30].

IR is closely related to systemic metabolism, and its relevance to other chronic diseases may also be mediated by metabolic abnormalities. Some respiratory specialists believe that the inflammatory response driving asthma may be induced in part by systemic metabolic abnormalities and that medications to treat IR may help control asthma [31]. A retrospective study based on electronic health records showed that glucagon-like peptide-1 receptor agonists were able to reduce the number of acute asthma exacerbations [32]. IR promotes the production of visceral fat, which is more closely associated with cardiometabolic risk factors than other obesity phenotypes and is considered a key factor in the prevalence of heart disease [33]. A study from the Czech Republic found that IR causes changes in cholesterol profiles and that cholesterol levels are negatively associated with insulin levels [34]. IR-induced hyperinsulinemia causes cholesterol deficiency, which induces nuclear factor kappa-B activation and promotes gastrointestinal tumorigenesis [35]. In addition, hyperinsulinemia itself is a possible mechanism for the development of gastric malignancy [35]. Previous studies from the United States have concluded that IR-related indices associated with the prevalence of CKD and can be used to predict the occurrence of CKD [13]. However, the results of our study do not support this conclusion. This difference may be due to the fact that the predominant cause of CKD in the United States associated is diabetes mellitus, whereas in China it is not. Previous studies have also confirmed the weak

predictive value of TyG and TyG-related indices for CKD in Chinese middle-aged and older adults [36].

We found that the association of some chronic diseases with IR was only significant in unadjusted Model 1 and not present in Models 2 and 3 (heart disease and TyG, asthma and eGDR). Also, the RCS analysis did not show nonlinear associations between them. A Chinese cohort study showed that TyG did not have an independent effect on heart disease risk, and their association was influenced by gender, diabetes, and BMI [37]. Our results are consistent with this finding. There are no specific studies on the association between asthma and eGDR, but previous studies have found that factors such as gender and obesity affect the association between TyG, TyG-BMI and asthma [38, 39]. From this, we hypothesized that the association between eGDR and asthma was similarly influenced by these factors.

In the ROC analysis, the IR-related indices had the highest predictive accuracy for dyslipidemia. TyG is superior to other IR-related indices for predicting the development of dyslipidemia in middle-aged and elderly Chinese persons. We hypothesize that this result may be related to the type of obesity in the Chinese population. Individuals with compound obesity in the middle-aged and elderly Chinese population have the highest risk of dyslipidemia [40], so BMI and waist circumference alone do not improve predictive accuracy.

In conclusion, this present study included a relatively large cohort of Chinese populations. To the best of our knowledge, this is the first study to simultaneously assess the association of five IR-related indices with nine chronic diseases. We demonstrate the association between IR-related indices and chronic diseases, especially metabolic diseases, and their predictive value. We also performed subgroup analyses stratified by different confounders and identified associations between IR-related indices and chronic diseases in different populations. For example, overweight individuals showed an increased risk of hyperuricemia when IR-related indices were elevated. Therefore, clinicians need to pay more attention to IR in the middle-aged and elderly population to improve the early diagnosis of chronic diseases.

However, some limitations of this study must also be taken into account. First, the results of this study were based on the calculation of IR-related indices at baseline, and the cross-sectional study design limited the inference of causality. Further prospective studies and longitudinal cohort studies using multiple IR-related indices calculations are needed to further explore the relationship between IR-related indices and chronic diseases. Second, due to the lack of data on insulin levels, this study was unable to analyze IR-related indices based on insulin levels, such as the Homeostasis Model Assessment of IR (HOMA-IR) and the Quantitative Insulin Sensitivity Check Index (QUICKI). Third, the data in this study were derived from the Chinese population, so the findings may not be extrapolated to other countries and regions. Finally, a number of residual confounders that are difficult to detect or assess may have influenced the conclusions of this study.

Conclusions

The results of the present study suggest that IR-related indices remain associated with several chronic diseases, especially metabolic diseases, after the exclusion of numerous confounding factors. Those individuals with IR have higher risk of chronic diseases. These findings can guide preventive measures and reduce the burden of chronic diseases by improving IR in middle-aged and older people.

Abbreviations

IR	Insulin resistance
TyG	Triglyceride glucose index
TyG-BMI	Triglyceride glucose-body mass index
TyG-WHtR	Triglyceride glucose-waist-to-height ratio
METS-IR	Metabolic score of IR
eGDR	Estimated glucose disposal rate
CHARLS	China Health and Retirement Longitudinal Study
FPG	Fasting plasma glucose
BMI	Body mass index
TG	Triglycerides
HDL-c	High-density lipoprotein cholesterol
HbA1c	Glycated hemoglobin A
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
RCS	Restricted cubic spline
ROC	Receiver operating characteristic
AUC	Area under the curve
HOMA-IR	Homeostasis Model Assessment of IR
QUICKI	Quantitative Insulin Sensitivity Check Index

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41043-025-00878-3.

Supplementary Material 1

Supplementary Material 2

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Author contributions

W.J. carried out the data collection, completed the statistical analysis and drafted the manuscript. Z.F. was responsible for the study design, provided statistical support. Z.F. and M. X. revised the manuscript. E.Q. assisted in data collection and statistical analysis. K.L. conceived and supervised the project and contributed to manuscript preparation. All authors approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
In accordance with the Declaration of Helsinki, Peking University examined and authorized the studies involving human subjects in the China Health and Retirement Longitudinal Study (CHARLS) (IRB00001052–11015). The patients/participants provided their written informed consent to participate in CHARLS. Our study used publicly available deidentified data from the CHARLS website (http://charls.pku.edu.cn/index.htm) and waived informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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