

RESEARCH

Open Access



Impact of estimated glucose disposal rate for identifying prevalent ischemic heart disease: findings from a cross-sectional study

Jin Xuan¹, Du Juan², Niu Yuyu³ and Ji Anjing^{4*}

Abstract

Background: Insulin resistance is one of the major mechanisms for cardiovascular events. Estimated glucose disposal rate (eGDR) has been demonstrated as a simple, accurate, and cost-effective estimator of insulin resistance. Our study aims to evaluate the correlation between eGDR and the prevalent IHD and assess the incremental value of eGDR for identifying prevalent IHD in the rural general population.

Methods: Our study enrolled 10,895 participants from a cross-sectional survey of a metabolic management program. The survey was conducted in the rural areas of southeastern China between October 2019 and April 2020. $eGDR = 21.158 - (0.09 * \text{waist circumference}) - (3.407 * \text{hypertension}) - (0.551 * \text{HbA1c})$.

Results: The prevalence of IHD was 4.20%. After adjusting for demographic, anthropometric, laboratory, and medical history covariates, each SD increase of eGDR brought a 25.9% risk reduction for prevalent IHD. After dividing eGDR into groups, the top group had a 58.9% risk reduction than the bottom group. Furthermore, smooth curve fitting demonstrated that the correlation between eGDR and prevalent IHD was linear in the whole range of eGDR. Additionally, AUC suggested that eGDR could significantly improve the identification of prevalent IHD by adding it to cardiovascular risk factors (0.703 vs. 0.711, P for comparison = 0.041). Finally, the category-free net reclassification index and integrated discrimination index also implicated the improvement from eGDR to identify prevalent IHD.

Conclusion: Our data demonstrated a significant, negative, and linear correlation between eGDR and prevalent IHD. Our findings could suggest the potential usefulness of eGDR to improve the identification of prevalent IHD in the rural general population.

Keywords: Epidemiology, Estimated glucose disposal rate, Insulin resistance, Ischemic heart disease

Introduction

Even with the condition of intensive medical care, ischemic heart disease (IHD) is still one of the dominant causes of mortality worldwide. The attributed death caused by IHD was 116.9 per 100,000 worldwide in 2017 [1]. Similarly, mortality from IHD in China also reached

124 per 100,000 in 2017, and the data displayed a 20.6% increase compared with that in 1990 [2]. Although the electrocardiogram is a readily available, cheap, and accurate examination, the correct identification of IHD (especially the stable IHD) through electrocardiogram requires systemic learning and long-term experience accumulation, which are currently absent for the village doctor in the rural areas of China. Accordingly, an objective and quantified parameter or indicator could be more friendly for them to facilitate and simplify the identification of IHD in the rural general population.

*Correspondence: jaj278288743@outlook.com

⁴ Department of Cardiology, Yuhuan Second People's Hospital, Huanbaozhong Road, Yuhuan, Zhejiang, China
Full list of author information is available at the end of the article



Insulin resistance (IR) is one of the primary mechanisms for cardiovascular events [3]. As a central mechanism, IR links together all components of metabolic syndrome, including hypertension, dyslipidemia, hyperglycemia, and central obesity, which are major risk factors for cardiovascular events [4]. Moreover, prior studies have demonstrated that IR itself is also an independent risk factor for IHD [5–7]. On the contrary, a published article has revealed that the prevention of IR could diminish the probability of myocardial infarction by about 42% in a population of young adults via a mathematical analysis [8]. Data from the lab have also demonstrated that IR and the following hyperinsulinemia could accelerate the development of cardiovascular events via stimulating vascular stiffness, promoting atherosclerotic plaque formation, enhancing thrombosis, inhibiting fibrinolysis, and maintaining the persistence of low-grade inflammation [3, 9]. Therefore, estimating the degree of IR could benefit the early identification of IHD. However, the current gold standard for IR requires specialized equipment, which is rarely available in primary care conditions. Accordingly, a simple, economical, and non-invasive method to achieve routine monitoring of IR is needed to improve the early identification of IHD in the rural general population.

Estimated glucose disposal rate (eGDR) was proposed to estimate the severity of IR [10, 11]. eGDR has been demonstrated to have high precision in estimating IR compared to the euglycemic hyperinsulinemic clamp approach [12]. Additionally, published data have revealed the usefulness of eGDR in predicting cardiovascular events in diabetic patients [13–16]. However, evidence about the association between eGDR and the prevalent IHD in the general population is still limited. Hence, our current analysis aims to evaluate the association between eGDR and the prevalent IHD and assess the value of eGDR to improve the identification of prevalent IHD in a rural general population.

Methods

Study population

The National Metabolic Management Center (MMC) is a metabolic care system conducted in China since 2016. Based on advanced medical equipment and telecommunication, it was funded to establish a standard and reproducible platform for diagnosing and managing metabolic disorders. Our current study derived from a branch cross-sectional survey of the MMC. The survey was conducted in the rural areas of eastern Zhejiang between October 2019 and April 2020. The survey adopted a clustered random sampling method. In general, 31 villages from Yuhuan city were randomly selected, and all permanent residents aged ≥ 40 years old without any exclusion

criterion were enrolled into our survey. The exclusion criteria included cancer, mental disorder, and pregnancy. Eventually, 11,316 subjects completed the survey. An additional 421 subjects were excluded in the present work due to missed data of covariates, and 10,895 subjects were finally enrolled into our current work (Fig. 1). The central ethics committee of Yuhuan second People's Hospital approved the study protocol of the survey, and the survey was conducted on the base of the Declaration of Helsinki.

Data collection and measurement

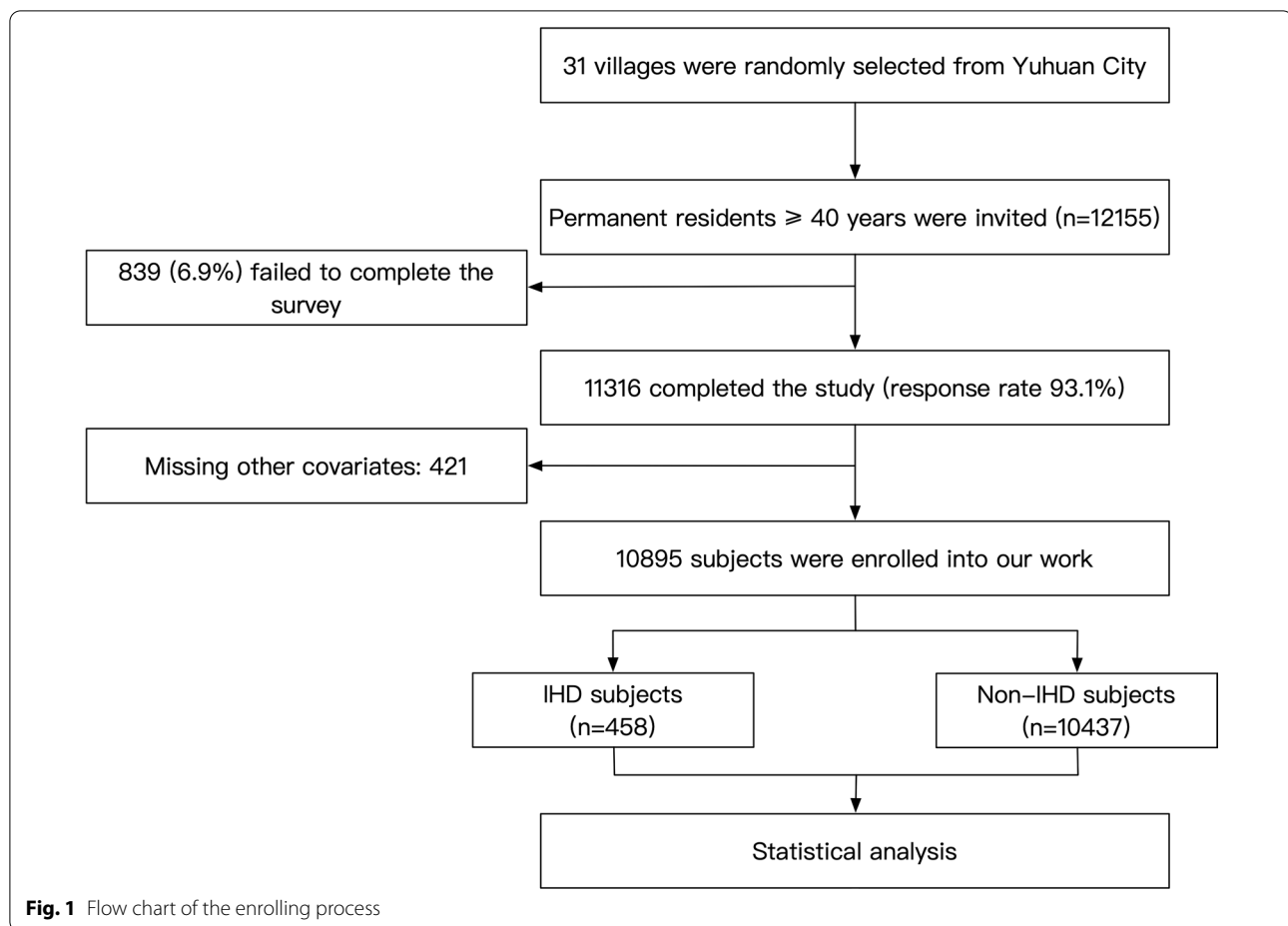
A team of medical students, epidemiologists, general practitioners, cardiologists, and neurologists was employed to conduct the data collection. All the members underwent an epidemiological course, passed a final examination, and were authorized to collect data. The study was conducted in clinics with large rooms designed for primary medical care by the local health commission.

The medical staff filled out a standardized questionnaire for every subject during a clinical visit. For demographic data, education level was defined into three groups: primary school or below, middle school, and high school or above. Frequent exercise was defined as an average of more than three hours of mild sweating activity per day. Family annual income was summarized into three levels: less than 5000 Chinese Yuan (CNY), 5000–20,000 CNY, or more than 20,000 CNY. Current smoking was determined as smoking more than 100 cigarettes within the past one year. Current drinking was defined as drinking an alcoholic beverage equal to or more than five times in the past one year.

Subjects were asked to wear light clothes and take off their shoes when measuring their anthropometric parameters. Weight and height were quantified into the nearest 0.1 kg and 0.1 cm by calibrated electric scales and stadiometers when the subjects were standing. Meanwhile, waist circumference (WC) was recorded at 1 cm above the umbilicus.

Blood pressure measurement was performed via calibrated electronic sphygmomanometers (HEM-7136; Omron, Kyoto, Japan). Measurement was conducted in the large, quiet room of the clinics. Subjects were required to avoid exercise, smoking, and caffeine intake within 30 min before the measurement. Every two measures had a two-minute interval between them. Three effective and consecutive recordings were used for each subject. The mean value of the three records was taken into our statistical analysis.

After about eight hours of fasting, fasting blood samples were collected from every subject. Blood samples were collected from the cephalic vein by veno-puncture and then stored in EDTA vacutainer tubes (Becton,



Dickinson and CO., Franklin Lakes, NJ, USA). The samples were centrifuged in site to isolate the serum from the whole blood. Then the samples were stored at -20°C . Subsequently, they were delivered to Yuhuan second people's hospital for laboratory analysis. Blood biochemical indices were quantified enzymatically by an auto-analyzer (Abbott Laboratories, Abbott Park, Illinois, USA). In addition, about 5% of the blood samples were randomly selected and re-tested at a certified 3rd party institute to enhance the accuracy of the laboratory test.

Twelve-leads ECG (Jinjiang, LEAD-7000c) was conducted for every subject in resting position for at least 10 s. Two cardiologists were employed to conduct and analyze the ECGs using callipers and magnifying glasses.

Definition

Anti-hypertensive therapy was determined as the usage of any anti-hypertensive drug in the past two weeks. Hypertension was defined as mean systolic blood pressure (mSBP) equal to or more than 140 mmHg and/or mean diastolic blood pressure (mDBP) equal to or more than 90 mmHg; subjects with self-reported anti-hypertensive

therapy were also regarded as hypertensive patients [17]. Anti-diabetic therapy was referred to the intake of any anti-diabetic drug in the past two weeks. And diabetes was defined as fasting plasma glucose (FPG) equal to or more than 7 mmol/L and/or glycated hemoglobin (HbA1c) $\geq 6.5\%$ and/or self-reported anti-diabetic therapy [18]. Obesity was defined as BMI $\geq 28\text{ kg/m}^2$ according to the Chinese guideline [19]. eGDR was calculated according to the following formula: $\text{eGDR} = 21.158 - (0.09 * \text{WC}) - (3.407 * \text{hypertension}) - (0.551 * \text{HbA1c})$. [hypertension (yes=1/no=0), HbA1c=HbA1c (%)] [11, 12]. Diagnosis of IHD relied on ECG results, medical records, and concrete medical examinations. Similar to the standard used in the Framingham study [20], copies of medical records for hospitalizations and outpatient cardiovascular diagnoses were obtained from subjects; two cardiologists reviewed the electrocardiogram and medical history independently to screen out the subjects suspect of IHD (ICD-10 code I 20 for angina pectoris, I 21 for acute myocardial infarction). For any subject suspected of having IHD, the cardiologists would further review the laboratory, imaging, and procedural data

(including coronary computational tomography angiography and coronary angiography) from the corresponding hospitals. Only subjects with concrete evidence were diagnosed with IHD. To ensure the accuracy of the diagnosis, two additional cardiologists would review the controversial cases to discuss for the final diagnosis.

Statistical analysis

Based on their distributions, continuous variables were shown as mean values (standard deviation, SD) or median (quartile 1–quartile 3). Categorical variates were summarized as frequency (percentage). The student's *t* test tested the difference between continuous variates for normal distribution or the Mann–Whitney test for skewed distribution. The Chi-square test and the Rank-sum test were used to assess the difference of categorical variates and ordinal categorical variates between groups, respectively. When analyzed as a continuous variable, eGDR was natural log-transformed before being included into statistical analysis due to its skewed distribution. Normalization of eGDR was conducted by z-score [(eGDR-mean value of eGDR)/ standard deviation (SD) of eGDR]. Furthermore, eGDR was categorized into four groups according to previously used cut-off levels [12, 21]. Multivariate logistic regression analysis investigated the independent association between eGDR and prevalent IHD. The results were shown as odds ratios (ORs) and 95% confidence intervals (95% CI). To confirm whether the correlation between eGDR and the prevalent IHD was linear in the full range of eGDR, we employed a generalized additive model with a spline smoothing function. We also conducted the subgroup analysis to assess whether some common cardiovascular risk factors could influence the association between eGDR and the prevalent IHD. The grouping factors included sex, age (grouped into <60 and ≥60 years), obesity, hypertension, and diabetes. Additionally, the present work conducted receiver operating characteristic (ROC) curve and reclassification analysis (includes category-free net reclassification index, NRI, and integrated discrimination index, IDI) to evaluate the value of eGDR for improving the identification of prevalent IHD. All the statistical analysis was conducted through statistical software packages R (<http://www.R-project.org>, The R Foundation), EmpowerStats (<http://www.empowerstats.com>, X&Y Solutions, Inc., Boston, MA), and SPSS 26.0 software (IBM Corp). Statistical significance was set as a 2-tailed *P* value less than 0.05.

Results

The characteristics of the 10,895 enrolled participants were summarized in Table 1. The prevalence of IHD was 4.20%. Regarding the demographic data, IHD patients had a higher age level, lower education and income levels,

a higher percentage of frequent exercise, and a lower percentage of current drinking. As for the anthropometric data, IHD patients had higher weight, BMI, WC, and blood pressure levels than non-IHD subjects. Similarly, laboratory data displayed that IHD patients had worse glucose and lipids conditions than their healthy counterparts. Moreover, IHD patients had higher rates of anti-hypertensive, anti-diabetic, and lipid-lowering therapy, and the prevalence of hypertension and diabetes were higher in the IHD group than in the non-IHD group. Finally, IHD patients also had a lower level of eGDR than non-IHD subjects.

The logistic regression revealed a significant and negative association between eGDR and the prevalent IHD; the results were displayed in Table 2. Without any adjustment, the risk of prevalent IHD decreased by 32.6% for every SD increment of eGDR. After adjusting for age, gender, education, income, and physical activity levels, current smoking and drinking conditions, each SD increase of eGDR only resulted in a 27.4% decrease of the risk of prevalent IHD (Model 1). After further adjustment of BMI, WC, TC, HDL-c, hypertension, diabetes, and lipid-lowering therapy, each SD increase of eGDR could only decrease the risk of prevalent IHD by 25.9%. We further divided eGDR into groups according to the standard in published articles. The prevalence of IHD was 8.5% in the lowest group, 9.4% in the second group, 4.5% in the third group, and 2.8% in the highest group. The 4th group had a 32.2% risk of prevalent IHD compared to the 1st group in the crude model. In model 1, the risk of prevalent IHD in the top group increased to 40.0% compared with the bottom group. In the fully adjusted model, the risk of prevalent IHD in the top group further inflated to 41.1% compared with the bottom group. Furthermore, we observed a significant trend towards a lower risk of prevalent IHD across the groups (all *P* for trend <0.001).

Our work further employed smooth curve fitting to verify the linear trend observed in Table 2; the result was displayed in Fig. 2. The plot demonstrated that the risk of prevalent IHD decreased proportionally with the increase of eGDR. Therefore, the correlation between eGDR and the prevalent IHD was linear in the whole range of eGDR.

Our current work also performed the subgroup analysis to evaluate whether the main finding from the logistic regression was robust in some common sub-populations (Fig. 3). The subgroups in our study included sex, age, obesity, diabetes, and hypertension. The logistic regression models in the subgroup analysis were adjusted for all covariates used in our main results (Model 2 of Table 2), except for the variate that was used to define subgroup. The results demonstrated that our major finding from the

Table 1 Characteristics of included participants

Variables	Total (n = 10,895)	IHD (458)	Non-IHD (n = 10,437)	P value
Age (years)	59.95 (10.07)	64.96 ± 8.17	59.73 ± 10.08	< 0.001
Male (%)	4379 (40.19)	175 (38.21)	4204 (40.28)	0.376
Education level (%)				0.005
Primary school or below	6445 (59.16)	302 (65.94)	6143 (58.86)	
Middle school	3483 (31.97)	115 (25.11)	3368 (32.27)	
High school or above	967 (8.88)	41 (8.95)	926 (8.87)	
Income (CNY) (%)				< 0.001
≤ 5000	4716 (43.29)	285 (62.23)	4431 (42.45)	
5000–20,000	4331 (39.75)	124 (27.07)	4207 (40.31)	
> 20,000	1848 (16.96)	49 (10.70)	1799 (17.24)	
Frequent exercise (%)	1806 (16.58)	166 (36.24)	1640 (15.71)	< 0.001
Current smoking (%)	2881 (26.44)	108 (23.58)	2773 (26.57)	0.156
Current drinking (%)	3065 (28.13)	90 (19.65)	2975 (28.50)	< 0.001
Height (cm)	159.38 (8.04)	158.81 ± 7.73	159.41 ± 8.05	0.117
Weight (kg)	63.17 (11.34)	64.19 ± 12.40	63.12 ± 11.29	0.048
BMI (kg/m ²)	24.81 (3.77)	25.38 ± 4.17	24.79 ± 3.75	< 0.001
WC (cm)	83.39 (10.22)	85.49 ± 11.87	83.29 ± 10.13	< 0.001
SBP (mmHg)	145.71 (23.62)	153.68 ± 23.60	145.36 ± 23.56	< 0.001
DBP (mmHg)	86.69 (11.93)	87.90 ± 12.25	86.64 ± 11.91	0.027
FPG (mmol/L)	5.74 (5.25–6.37)	6.05 (5.49–6.88)	5.73 (5.24–6.35)	< 0.001
HbA1c (%)	5.40 (5.10–5.80)	5.50 (5.10–6.00)	5.40 (5.10–5.80)	0.001
TC (mmol/L)	5.02 (4.38–5.74)	5.12 (4.35–5.98)	5.01 (4.38–5.73)	0.151
TG (mmol/L)	1.29 (0.91–1.89)	1.41 (1.00–1.99)	1.29 (0.90–1.89)	< 0.001
HDL-C (mmol/L)	1.79 (1.38–2.43)	1.50 (1.23–1.98)	1.80 (1.39–2.45)	< 0.001
LDL-C (mmol/L)	2.18 (1.51–3.00)	2.50 (1.82–3.10)	2.16 (1.50–3.00)	< 0.001
Anti-hypertensive therapy (%)	2337 (21.45)	230 (50.22)	2107 (20.19)	< 0.001
Anti-diabetic therapy (%)	579 (5.31)	55 (12.01)	524 (5.02)	< 0.001
Lipid-lowering therapy (%)	215 (1.97)	43 (9.39)	172 (1.65)	< 0.001
Hypertension (%)	6602 (60.60)	363 (79.26)	6239 (59.78)	< 0.001
Diabetes (%)	1767 (16.22)	126 (27.51)	1641 (15.72)	< 0.001
eGDR	8.04 (6.78–10.62)	7.21 (6.03–8.74)	8.08 (6.81–10.66)	< 0.001

Data were displayed as mean (SD), median (quartile 1–quartile 3), and numbers (percentage) according to their data type and distribution

IHD ischemic heart disease, CNY Chinese currency, BMI body mass index, WC waist circumference, SBP systolic blood pressure, DBP diastolic blood pressure, FPG fasting plasma glucose, HbA1c glycated hemoglobin, TC total cholesterol, TG triglyceride, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, eGDR estimated glucose disposal rate

entire population was robust in these subgroups (all *P* for interaction > 0.05).

To assess the potential usefulness of eGDR to identify the prevalent IHD in the general population, we further conducted ROC and reclassification analysis; the results were shown in Table 3. The AUC of eGDR alone for identifying the prevalent IHD was 0.620 (95% CI 0.611–0.629, *P* < 0.001). After introducing eGDR into established IHD risk factors (age, gender, current smoking and drinking conditions, BMI, WC, TC, HDL-c, hypertension, diabetes, and lipid-lowering therapy), the results displayed a significant improvement in the identification of prevalent IHD (AUC: 0.703 vs. 0.711, *P* for comparison = 0.041).

Additionally, category-free NRI (0.209, 95% CI 0.121–0.297, *P* < 0.001) and IDI (0.004, 95% CI 0.002–0.007, *P* < 0.001) also displayed significant values for eGDR to improve the identification of the prevalent IHD.

Discussion

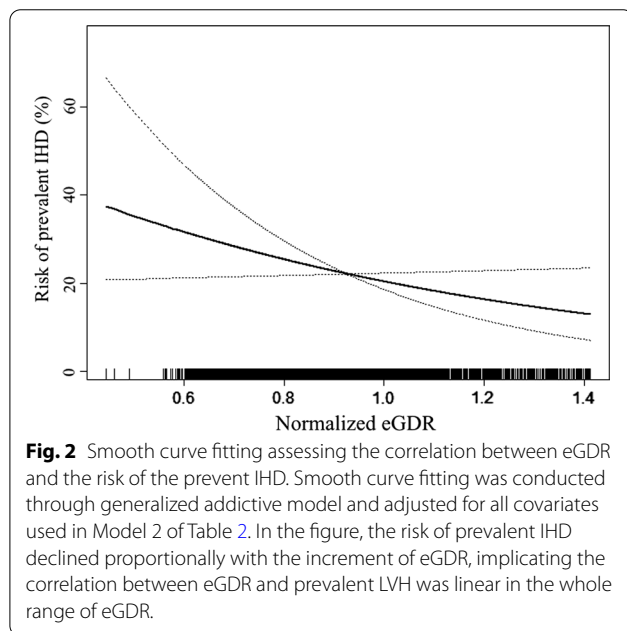
Our current work demonstrated a significant, negative, and linear correlation between eGDR and prevalent IHD, implicating a positive and significant correlation between the degree of insulin resistance and prevalent IHD. Furthermore, our study demonstrated the correlation between eGDR and prevalent IHD was robust in several common subpopulations. Additionally, our

Table 2 Multivariate logistic regression evaluating the correlation between eGDR and prevalent IHD

Variables	Prevalence of IHD (%)	Odds ratio (95% CI)					
		Crude	P value	Model 1	P value	Model 2	P value
eGDR (per 1 SD increase)	–	0.674 (0.619, 0.733)	<0.001	0.726 (0.664, 0.794)	<0.001	0.741 (0.636, 0.864)	<0.001
Groups of eGDR							
eGDR < 4	11 (8.5)	Reference		Reference		Reference	
4 ≤ eGDR < 6	103 (9.4)	1.135 (0.593, 2.174)	0.702	1.140 (0.589, 2.203)	0.698	1.155 (0.586, 2.276)	0.677
6 ≤ eGDR < 8	187 (4.5)	0.520 (0.276, 0.980)	0.043	0.557 (0.292, 1.060)	0.075	0.582 (0.285, 1.189)	0.138
8 ≤ eGDR	157 (2.8)	0.322 (0.170, 0.609)	<0.001	0.400 (0.209, 0.766)	0.006	0.411 (0.189, 0.896)	0.025
P for trend	–		<0.001		<0.001		<0.001

Crude model: no adjustment; Model 1: adjusted for age, sex, education level, income level, physical activity, current smoking, current drinking; Model 2: Model 1 + BMI, WC, TC, HDL, hypertension, diabetes, and lipid-lowering therapy

eGDR estimated glucose disposal rate, IHD ischemic heart disease, CI confidence interval, SD standard deviation, BMI body mass index, WC waist circumference, TC total cholesterol, HDL-C high-density lipoprotein cholesterol



analysis revealed a significant improvement in identifying prevalent IHD when adding eGDR into several cardiovascular risk factors. The present analysis could implicate a potential correlation between eGDR, and the underlying insulin resistance, and the risk of the prevalent IHD. Furthermore, our study could also suggest the potential value of eGDR in improving the identification of prevalent IHD.

Our findings confirmed our hypothesis about the association between eGDR and prevalent IHD. After adjusting for demographic, anthropometric, laboratory, and medical history data, the logistic regression revealed a negative and significant correlation between eGDR and the prevalent IHD. Every SD increase of eGDR could

diminish the risk of prevalent IHD by 25.9%. Because of the negative relationship between eGDR and the severity of IR, our data implicate the positive correlation between IR and the risk of the prevalent IHD. Moreover, by dividing eGDR into groups according to published criteria, we observed a linear trend towards a higher risk of the prevalent IHD across groups. Additionally, the smooth curve fitting demonstrated that the correlation between eGDR and the prevalent IHD was linear in the whole range of eGDR, implicating the risk decreases proportionally with the increment of eGDR. Therefore, eGDR may act as a linear indicator for the risk of the prevalent IHD. Finally, the results from the subgroup analysis implicate that the negative association between eGDR and the prevalent IHD is not influenced by sex, age, obesity, hypertension, and diabetes. Therefore, applying our primary result to these sub-populations could be reasonable and feasible.

To assess the value of eGDR to improve the identification of prevalent IHD in the general population, our study employed ROC and reclassification analysis. As for ROC analysis, eGDR alone had a moderate AUC, suggesting the limited value of eGDR alone to identify the prevalent IHD. However, by adding eGDR to several cardiovascular risk factors, we observed a significant improvement in identifying the prevalent IHD (AUC: 0.703 vs. 0.711, P for comparison = 0.041). Nevertheless, although ROC analysis is the most popular approach to assessing the value of a novel marker, ROC analysis still has its disadvantage. ROC analysis has a low sensitivity to recognize the usefulness of a novel marker to improve the identification of prevalent diseases [22]. ROC analysis focuses on the comparison of the ability of models to identify the risk of prevalent diseases, but it pays little attention to whether adding a new marker into existed risk factors could improve the identification of prevalent diseases [23]. Therefore,

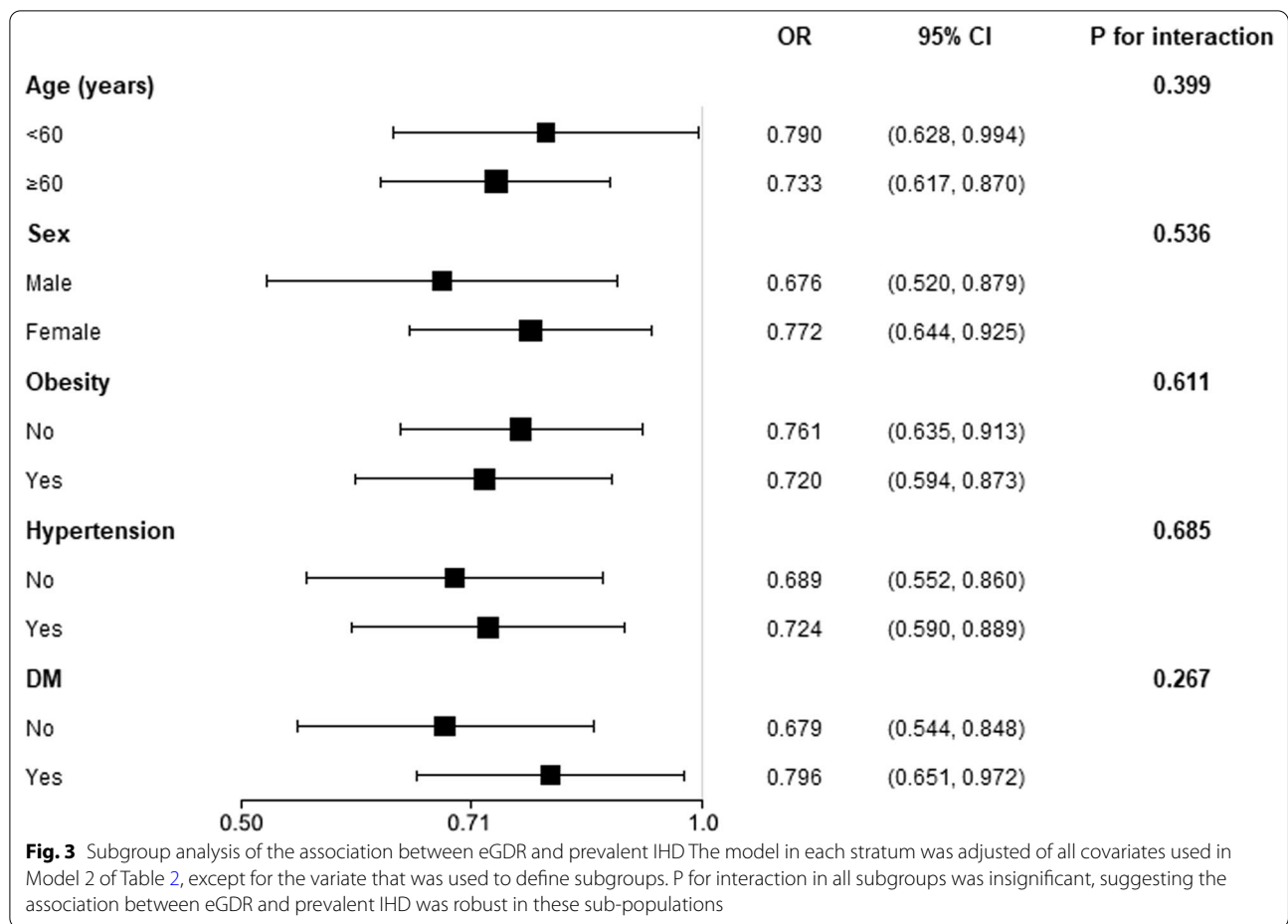


Table 3 ROC and reclassification analysis investigating the usefulness of eGDR to optimize the identification of prevalent IHD

Model	AUC (95% CI)	P value	P for comparison	NRI (category free)	P value	IDI	P value
eGDR	0.620 (0.611, 0.629)	< 0.001	–	–	–	–	–
Clinical risk factors*	0.703 (0.695, 0.712)	< 0.001	–	–	–	–	–
Clinical risk factors + eGDR	0.711 (0.703, 0.720)	< 0.001	0.041	0.209 (0.121, 0.297)	< 0.001	0.004 (0.002, 0.007)	< 0.001

*Clinical risk factors: age, sex, current smoking, current drinking, BMI, WC, TC, HDL, hypertension, diabetes, and lipid-lowering therapy

ROC receiver operating characteristic curve; eGDR estimated glucose disposal rate; IHD ischemic heart disease; AUC area under the curve, CI confidence interval; NRI net reclassification improvement, IDI integrated discrimination index, BMI: body mass index, WC waist circumference, TC: total cholesterol, HDL-C: high-density lipoprotein cholesterol

ROC analysis alone may not be able to evaluate the usefulness of a new marker to identify prevalent IHD comprehensively. Accordingly, scientists have begun to use reclassification analysis to investigate the incremental value of new markers to identify prevalent diseases [24–26]. In the current analysis, we also employed reclassification analysis to assess the value of eGDR. Both category-free NRI and IDI were significant, suggesting the potential incremental value of eGDR to

improve the identification of the prevalent IHD. Therefore, both ROC and reclassification analysis bolstered the potential incremental value of eGDR. Hence, general practitioners in rural primary care conditions could achieve more precise identification of prevalent IHD than ever before by applying eGDR to daily clinical practice.

It is our obligation to elucidate the significance of applying eGDR to facilitate the identification of the

prevalent IHD. In China, although the doctors from hospitals in large cities are well-educated and specialized, the primary practitioners, especially the village doctors in rural areas, still lack systemic medical education [27]. Due to the low income, village doctor is usually occupied by middle-aged people with the lowest medical education. Therefore, most of them did not receive systematic electrocardiogram training; thereby, they are unable to identify IHD, especially the stable IHD, independently. Due to this condition, an objective and quantified parameter or indicator could be more friendly for them to facilitate the identification of prevalent IHD in the rural population. From this view and combining our findings in the current study, we believe the village doctor in the rural areas of China could calculate eGDR to facilitate the identification of prevalent IHD in the rural general population.

When interpreting our findings, it is necessary to mention that the prevalence of IHD was relatively lower than those in similar surveys. Nevertheless, according to a published Chinese national survey of cardiovascular diseases, the prevalence of IHD in Chinese females and males was 0.51% and 0.74%, respectively [28]. The survey revealed that the prevalence of IHD in subjects aged ≥ 40 years old ranged from 0.28 to 2.41%. Moreover, the 2018 China cardiovascular diseases report demonstrated that the prevalence of IHD maintained at this level in the past ten years [29]. Additionally, the prevalence of IHD in our survey was similar to the prevalence in several Chinese cohorts [30–32]. Therefore, we believe the results from our study were still reliable but needed to be confirmed in other populations.

From the description of the characteristic data in Table 1, we observed that the IHD group had an approximately 80% prevalence of hypertension, and the median glycated hemoglobin level was 5.50%. This phenomenon may indicate that eGDR may predominantly depend on the presence of hypertension rather than diabetes. However, when comparing our results with the results from existing literatures, we found our observation is consistent with previous findings. In Penno et al.'s study, subjects with $eGDR < 4.14$ had a hypertension prevalence of 99.5%, subjects with eGDR value between 4.15 and 5.34 also had a hypertension prevalence of 98.7%, and subjects with $eGDR \geq 5.34$ had a hypertension prevalence of 52.8% [11]; In their work, they also used euglycemic hyperinsulinemic clamp test to exam the correlation between eGDR and the level of measured glucose disposal rate, the results demonstrated that the correlation of eGDR with measured glucose disposal rate was highly significant ($r = 0.624$, $P < 0.001$). In another study assessing the value of eGDR, the prevalence of anti-hypertensive therapy reached 97.9% in subjects with $eGDR < 4$; On

the contrary, the prevalence of anti-hypertensive therapy was only 41.0% and 1.1% in subjects with eGDR 6–8 and > 8 , respectively [13]. In this research, the researcher also observed a close correlation between eGDR and the results of euglycemic hyperinsulinaemic clamp ($r = 0.73$). From the view of mechanisms, insulin resistance could lead to hypertension through multiple mechanisms; and multiple studies have identified the association between insulin resistance and the exacerbated risk of hypertension in the general population [33]. Based on the above information, we believe the high prevalence of hypertension in the IHD group, which had a low eGDR level, could still be reasonable, but further studies are still needed to assess whether the high prevalence of hypertension will influence the accuracy of eGDR to estimate the actual level of insulin resistance.

It is essential to notice the limitations in our current work when interpreting our findings. Firstly, our study originated from cross-sectional data of an epidemiological survey. Due to the pandemic of COVID-19, the follow-up data is unavailable until now. Therefore, our results only suggest the association between eGDR, and the underlying IR, and the prevalent IHD. The longitudinal relationship still needs prospective cohorts to confirm. Secondly, our subjects were sampled from a natural population in southeastern China. Hence, the findings from our work may not be applicable to people of different races and socioeconomic conditions and live in different geographic conditions; In other words, the external validity of the current findings still needs further studies to verify. Thirdly, the definition of IHD used in our work could overlook the asymptomatic obstructive IHD in the population. This is a major limitation of our manuscript. However, as an observational epidemiologic study with a relatively large sample size, it is not feasible to perform coronary computational tomograph or coronary angiography for all subjects. Studies with optimized definitions of IHD which can identify asymptomatic obstructive IHD are warranted to verify our conclusions. Lastly, because of the observational design of our survey, some unrecorded covariates may cast residual confounding and introduce bias into our results. For example, we measured the renal function only in a part of the participants. In the current analysis, most subjects were lack of renal function data. If we adjusted renal function in the current analysis, the sample size would shrink significantly, leading to a lack of statistical power. Accordingly, more longitudinal studies with more comprehensive and complete information collection are needed to verify the association between eGDR and the risk of prevalent IHD.

Conclusion

In general, our work demonstrated a negative, linear, and robust association between eGDR, a simple surrogate of IR, and the risk of the prevalent IHD in a rural general population. Moreover, our data could suggest the potential value of eGDR to improve the identification of the prevalent IHD in the general population, implicating the potential usefulness of eGDR to serve as a rapid, simple, and cost-effective marker to improve the identification of prevalent IHD in rural areas.

Acknowledgements

We acknowledge the colleges from Yuhuan second people's hospital for their efforts in completing the present survey.

Authors' contributions

XJ participated the survey, conducted the statistical analysis, and wrote the draft of the present article. DJ and NYY participated in the conduction of the survey. JAJ reviewed and revised the draft and proofed it for submission. All authors reviewed the revised manuscript. All authors read and approved the final manuscript.

Funding

None.

Data availability

The datasets generated and/or analyzed during the current study are not publicly available currently because the survey is part of an ongoing cohort, which has a limited access period due to the regulation of local technology bureau. However, the datasets will be available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All methods used in the survey were carried out in accordance with relevant guidelines and regulations, and the survey was conducted on the base of the Declaration of Helsinki. The central ethics committee of Yuhuan second people's hospital approved the study protocol of the survey. Informed consent was obtained from all subjects and/or their legal guardian(s).

Consent for publication

Every participant provided a written consent to publish their information collected by this survey, excluding their name and ID number.

Competing interests

The authors report no conflict of interest.

Author details

¹Department of Cardiology, The Second Affiliated Hospital of Shandong, University of Traditional Chinese Medicine, Jinan, Shandong, China. ²Department of Cardiology, Rizhao Hospital of Traditional Chinese Medicine, Rizhao, Shandong, China. ³Department of Cardiology, Xinxiang First People's Hospital, Xinxiang, Henan, China. ⁴Department of Cardiology, Yuhuan Second People's Hospital, Huanbaozhong Road, Yuhuan, Zhejiang, China.

Received: 9 March 2022 Accepted: 22 June 2022

Published online: 20 August 2022

References

- GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392(10159):1736–88.
- Zhou M, Wang H, Zeng X, Yin P, Zhu J, Chen W, Li X, Wang L, Wang L, Liu Y, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019. 394(10204):1145–58.
- Laakso M, Kuusisto J. Insulin resistance and hyperglycaemia in cardiovascular disease development. *Nat Rev Endocrinol*. 2014;10(5):293–302.
- Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC, Jr. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120(16):1640–45.
- Jeppesen J, Hansen T, Rasmussen S, Ibsen H, Torp-Pedersen C, Madsbad S. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease: a population-based study. *J Am Coll Cardiol*. 2007;49(21):2112–9.
- Bressler P, Bailey SR, Matsuda M, DeFronzo RA. Insulin resistance and coronary artery disease. *Diabetologia* 1996;39(11):1345–1350.
- Chen W, Wang S, Lv W, Pan Y. Causal associations of insulin resistance with coronary artery disease and ischemic stroke: a Mendelian randomization analysis. *BMJ Open Diabetes Res Care*. 2020;8(1):e001217–25.
- Eddy D, Schlessinger L, Kahn R, Peskin B, Schiebinger R. Relationship of insulin resistance and related metabolic variables to coronary artery disease: a mathematical analysis. *Diabetes Care*. 2009;32(2):361–66.
- Hill MA, Yang Y, Zhang L, Sun Z, Jia G, Parrish AR, Sowers JR. Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism*. 2021;119:154766.
- Williams KV, Erbey JR, Becker D, Arslanian S, Orchard TJ. Can clinical factors estimate insulin resistance in type 1 diabetes? *Diabetes*. 2000;49(4):626–32.
- Penno G, Solini A, Orsi E, Bonora E, Fondelli C, Trevisan R, Vedovato M, Cavalot F, Zerbini G, Lamacchia O, et al. Insulin resistance, diabetic kidney disease, and all-cause mortality in individuals with type 2 diabetes: a prospective cohort study. *BMC Med*. 2021;19(1):66.
- Nyström T, Holzmann MJ, Eliasson B, Svensson AM, Sartipy U. Estimated glucose disposal rate predicts mortality in adults with type 1 diabetes. *Diabetes Obes. Metab*. 2018;20(3):556–63.
- Zabala A, Darsalia V, Lind M, Svensson AM, Franzén S, Eliasson B, Patrone C, Jonsson M, Nyström T. Estimated glucose disposal rate and risk of stroke and mortality in type 2 diabetes: a nationwide cohort study. *Cardiovasc Diabetol*. 2021;20(1):202.
- Helliwell R, Warnes H, Kietsiriroje N, Campbell M, Birch R, Pearson SM, Ajjan RA. Body mass index, estimated glucose disposal rate and vascular complications in type 1 diabetes: Beyond glycated haemoglobin. *Diabet Med*. 2021;38(5):e14529.
- O'Mahoney LL, Kietsiriroje N, Pearson S, West DJ, Holmes M, Ajjan RA, Campbell MD. Estimated glucose disposal rate as a candidate biomarker for thrombotic biomarkers in T1D: a pooled analysis. *J Endocrinol Invest*. 2021;44(11):2417–26.
- Girgis CM, Scalley BD, Park KE. Utility of the estimated glucose disposal rate as a marker of microvascular complications in young adults with type 1 diabetes. *Diabetes Res Clin Pract*. 2012;96(3):e70–72.
- James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Oggedegbe O, et al. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507–20.
- Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003;26(Suppl 1):S5–20.
- Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. *Biomed Environ Sci*. 2004;17(Suppl):1–36.
- Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97(18):1837–47.
- Nyström T, Holzmann MJ, Eliasson B, Svensson AM, Kuhl J, Sartipy U. Estimated glucose disposal rate and long-term survival in type 2 diabetes after coronary artery bypass grafting. *Heart Vessels*. 2017;32(3):269–78.

22. Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation*. 2007;115(7):928–35.
23. Pickering JW, Endre ZH. New metrics for assessing diagnostic potential of candidate biomarkers. *Clin J Am Soc Nephrol*. 2012;7(8):1355–64.
24. Pencina MJ, D'Agostino RB, Sr., D'Agostino RB, Jr., Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med*. 2008;27(2):157–72; discussion 207–112.
25. Pencina MJ, D'Agostino RB, Sr., Steyerberg EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med*. 2011;30(1):11–21.
26. Grunkemeier GL, Jin R. Net reclassification index: measuring the incremental value of adding a new risk factor to an existing risk model. *Ann Thorac Surg*. 2015;99(2):388–92.
27. Li X, Krumholz HM, Yip W, Cheng KK, De Maeseneer J, Meng Q, Mossialos E, Li C, Lu J, Su M, et al. Quality of primary health care in China: challenges and recommendations. *Lancet*. 2020;395(10239):1802–12.
28. Yang ZJ, Liu J, Ge JP, Chen L, Zhao ZG, Yang WY. Prevalence of cardiovascular disease risk factor in the Chinese population: the 2007–2008 China National Diabetes and Metabolic Disorders Study. *Eur Heart J*. 2012;33(2):213–20.
29. Ma LY, Chen WW, Gao RL, Liu LS, Zhu ML, Wang YJ, Wu ZS, Li HJ, Gu DF, Yang YJ, et al. China cardiovascular diseases report 2018: an updated summary. *J Geriatr Cardiol*. 2020, 17(1):1–8.
30. Wang Y, Li Y, Liu X, Zhang H, Abdulai T, Tu R, Tian Z, Qian X, Jiang J, Qiao D, et al. Prevalence and influencing factors of coronary heart disease and stroke in chinese rural adults: the Henan rural cohort study. *Front Public Health*. 2019;7:411.
31. Chen LZ, Ding RJ, Shi QT, Hu DY. Risk factors and prevalence of cardiovascular disease of rural residents in Xianghe of Hebei province. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2013;41(10):882–5.
32. He L, Tang X, Song Y, Li N, Li J, Zhang Z, Liu J, Yu L, Xu H, Zhang J, et al. Prevalence of cardiovascular disease and risk factors in a rural district of Beijing, China: a population-based survey of 58,308 residents. *BMC Public Health*. 2012;12:34.
33. Wang F, Han L, Hu D. Fasting insulin, insulin resistance and risk of hypertension in the general population: a meta-analysis. *Clin Chim Acta*. 2017;464:57–63.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

