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Association of estimated glucose disposal rate with incident cardiovascular disease under different metabolic and circadian rhythm states: findings from a national population-based prospective cohort study

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Abstract

Background Recent studies have shown that both metabolic syndrome and circadian rhythm syndrome are firmly associated with the occurrence of cardiovascular disease (CVD), with insulin resistance playing a significant role. The estimated glucose disposal rate (eGDR) is considered to be a reliable surrogate marker for insulin resistance. However, the relationship between eGDR and CVD under different metabolic and circadian rhythm states has not been thoroughly studied, and large-scale prospective cohort studies are needed to clarify this relationship.

Methods This study is based on the China Health and Retirement Longitudinal Study (CHARLS), recruiting individuals aged 45 and above with complete eGDR data. The eGDR was calculated by the formula: eGDR(mg/kg/min) = 21.158 − (0.09 × WC) − (3.407 × hypertension) − (0.551 × HbA1c) [WC (cm), hypertension (yes = 1/no = 0), and HbA1c (%)] (Zabala et al. in Cardiovasc Diabetol 20(1):202; 2021).Participants were divided into four subgroups based on the quartiles (Q) of eGDR.The cumulative incidence rates and hazard ratios (HR) with 95% confidence intervals (CI) were calculated, with the lowest eGDR quartile (representing the highest degree of insulin resistance) as the reference. Participants were further divided into subgroups based on the diagnosis of Metabolic syndrome (MetS) or circadian syndrome (CircS) to explore the relationship between eGDR and CVD under different metabolic and circadian rhythm conditions. The dose–response relationship between eGDR and CVD incidence was investigated using a restricted cubic spline (RCS) based on a Cox regression model. Receiver operating characteristic (ROC) curves were generated to assess the predictive value of eGDR for CVD incidence. A clinical decision curve analysis (DCA) was also conducted to assess the clinical utility of the basic model.

Results 6507 participants were included, with a median age of 58 years [52 years, 64 years], and 55% were female. Over a median follow-up duration of 87 months, 679 first-episode CVD events were recorded, including heart disease and stroke. The RCS curves demonstrated a significant dose–response relationship between eGDR and the incidence

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of first-presentation CVD in different metabolic and circadian rhythm subgroups (all P-values < 0.001, non-linearity P > 0.05). eGDR exhibited a significant linear relationship with all outcomes (non-linearity P < 0.05). The Kaplan–Meier cumulative incidence curves showed that as eGDR levels increased, the cumulative incidence rates of first CVD, heart disease, and stroke gradually decreased from Q1 to Q4 groups. Significant differences were observed across all metabolic and circadian rhythm subgroups (log-rank test P < 0.001). Through the Cox proportional hazards model, we confirmed a significant association between baseline eGDR levels and first-onset CVD, heart disease, and stroke. Subgroup analyses indicated that the predictive ability of eGDR for CVD risk varied across different Body mass index (BMI) (P for interaction = 0.025) and age (P for interaction = 0.045) subgroups. Mediation analysis revealed that CircS partially mediated this association. Furthermore, time-dependent ROC curves demonstrated the potential of eGDR as a predictor of CVD risk, revealing possible differences in the model's application across different cardiovascular conditions.

Conclusion eGDR is an independent predictor of CVD risk, with lower eGDR levels being closely associated with a higher risk of CVD (including heart disease and stroke). In populations with MetS or CircS, the association between lower eGDR levels and increased risk is more pronounced.

Keywords Insulin resistance, Cardiovascular disease, Estimated glucose disposal rate, Metabolic syndrome, Circadian rhythm syndrome

Introduction

Cardiovascular disease is the primary cause of illness and death worldwide, significantly impacting healthcare systems and individual well-being. Over the last three decades, the burden of CVD has grown consistently, with a 92.3% rise in total prevalence and a 53.7% increase in the number of deaths [2].

Metabolic syndrome (MetS) is a collection of risk factors and associated conditions that contribute to cardiovascular disease [3], including elevated blood pressure, dyslipidemia (characterized by high triglycerides and low high-density lipoprotein cholesterol), increased fasting glucose levels, and central obesity [4]. It is a significant contributor to non-communicable diseases such as obesity, type 2 diabetes, cardiovascular disease, cancer, and mood disorders, imposing substantial health and socioeconomic costs in most countries. Research indicates that metabolic syndrome is frequently associated with comorbidities like sleep disorders, depression [5–7], cognitive impairment, and non-alcoholic fatty liver disease (NAFLD) [8, 9]. Given this, circadian rhythm disturbances have been proposed as a potential common cause of metabolic syndrome. Circadian rhythm syndrome (CircS) is characterized by the presence of at least four out of the following seven features: enlarged waist circumference, high triglyceride levels, low high-density lipoprotein (HDL) cholesterol, high blood pressure, elevated fasting glucose, insufficient sleep duration (less than 6 h per day), and symptoms of depression [10]. Studies such as the one by Shi et al. suggest circadian rhythm syndrome strongly predicts CVD [11, 12].

Insulin resistance (IR) is an independent risk factor for cardiovascular disease, as it elevates cardiovascular risk by facilitating the onset of metabolic disorders (such as hyperglycemia, hypertension, and dyslipidemia), contributing to endothelial dysfunction, and promoting low-grade inflammation [14].IR is defined by a reduced sensitivity or responsiveness of tissues to circulating insulin, which plays a crucial role in developing metabolic syndrome [15]. Meanwhile, circadian rhythm disruptions can impair glucose homeostasis, reducing insulin sensitivity. Disruptions in circadian rhythms may act as a mediator in the relationship between insulin resistance and cardiovascular disease. Moreover, it is essential to study insulin resistance in different populations under varying metabolic and circadian rhythm statuses to predict CVD events [16]. The estimated glucose disposal rate is an innovative, non-insulin-based surrogate marker for insulin resistance, calculated using a combination of waist circumference (WC), hypertension, and glycated hemoglobin (HbA1c) [17]. Unlike traditional measures such as the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), which focuses solely on fasting glucose and insulin levels, eGDR incorporates blood pressure and waist circumference, reflecting an individual's long-term physical condition. At the same time, glycated hemoglobin (HbA1c) captures extended blood glucose control. This makes eGDR a more comprehensive indicator of metabolic health [1]. Previous research indicates that eGDR (estimated Glucose Disposal Rate) is minimally affected by single glucose fluctuations and less influenced by factors such as diet, exercise, medication, or emotional changes [18]. This demonstrates the stability of eGDR as a predictive marker. Moreover, multiple studies have shown that eGDR has more substantial predictive power for cardiovascular disease risk [19], especially in

non-diabetic populations [21, 22]. Research indicates that eGDR is more effective than traditional methods, which rely solely on fasting glucose or insulin levels, in predicting complications such as atherosclerosis and heart disease [22]. For example, eGDR has been shown to outperform HOMA-IR in assessing cardiovascular risk in patients with type 1 diabetes [20]. Additionally, prior research has found that eGDR provides greater accuracy in evaluating insulin resistance [23], further highlighting its broader clinical relevance.

Nevertheless, the connection between eGDR and CVD across various metabolic conditions and circadian rhythm states still needs to be studied more. Therefore, in this study, we aim to assess the relationship between insulin resistance (evaluated by eGDR) and the risk of new-onset cardiovascular diseases (stroke or cardiac events) in middle-aged and elderly Chinese populations under varying metabolic and circadian rhythm conditions.

Methods

Study design and population

We extracted data from the CHARLS cohort study of the Chinese population aged 45 and above [24]. Detailed information on the study design and enrollment criteria has been reported previously. In short, the baseline survey was conducted from June 2011 to March 2012, and a nationally representative sample of 17,708 individuals from 10,257 households was selected. These participants were regularly followed up every two years with face-to-face interviews conducted by trained interviewers using computer-assisted guidance. Subsequent waves of follow-up were conducted in 2013, 2015, 2018, and 2020, but the latest wave of data has not yet been released. In this study, we included data from 2013, 2015, and 2018, with 6,507 participants included in the analysis, further divided into four subgroups based on the quartiles (Q) of eGDR. Another 11,201 participants were excluded from the study for the following reasons: loss to follow-up by 2018 and participants who did not have fasting blood samples (n = 7,720); missing baseline information and no blood sample provided in 2011 (n = 2,639); diagnosed at baseline as age < 45 (n = 235) and cancer (n = 47), or age data unavailable (n = 298); (Supplementary File 1, Fig. 1). The Peking University Ethics Review Committee approved the CHARLS protocol, and all CHARLS participants provided written informed consent.

Exposure and related definitions

The calculation formula for eGDR [mg/(kg·min)] is: eGDR = 21.158—[0.09 × waist circumference (cm)]—[3.407 × hypertension (yes/no)]—[0.551 × glycated hemoglobin (HbA1c, %)]. The lower the eGDR, the poorer the body's ability to process glucose and a higher level of insulin resistance. '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 [25]. MetS is defined as having ≥ 3 of the following components: increased waist circumference (≥ 85 cm for men, ≥ 80 cm for women), hypertension (systolic blood pressure ≥ 130 and diastolic blood pressure ≥ 85 mmHg) or antihypertensive treatment, high lipoprotein cholesterol (LDL) cholesterol (≥ 130 mg/dL) or treatment for high LDL, low HDL cholesterol (men < 40 mg/dL, women < 50 mg/dL) or treatment for low HDL cholesterol, and high triglycerides (≥ 150 mg/dL) or treatment for high triglycerides. Lipid-lowering agents were based on self-report use of Western medication for the treatment of dyslipidemia. CircS is defined based on seven components: short sleep duration (< 6 h/day), depression, and the five components

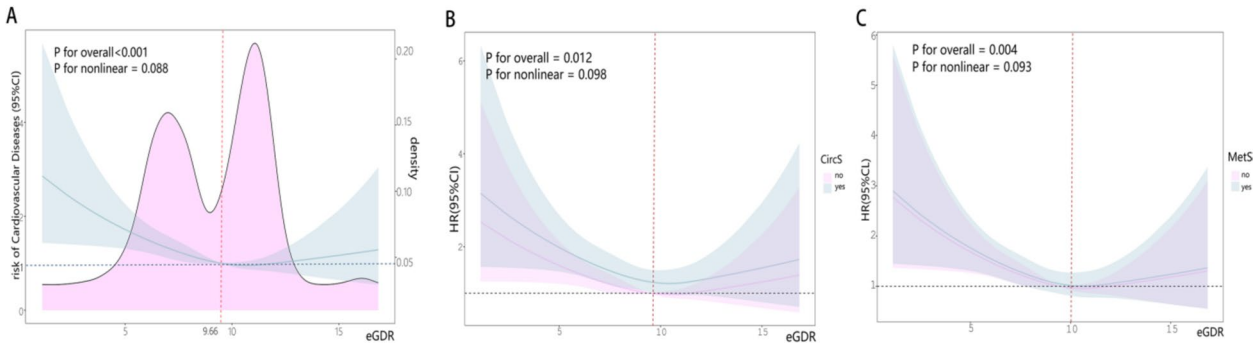

Fig. 1 The restricted cubic spline curves for CVD based on eGDR [for all participants (**A**), stratified by CircS (**B**), and stratified by MetS(**C**)]. Hazard ratios are indicated by solid lines and 95% CIs by shaded areas. The hori-zontal dotted line represents the hazard ratio of 1.0. The adjusted models adjusted age, gender, marital, education, smoking, drinking, local, HDL, BUN, UA, hsCRP, Chronic kidney disease

used to define MetS. Individuals with a score of ≥ 4 are considered to have CircS [13, 26, 27].

Covariates

We collected demographic information of participants from the CHARLS database. Specifically, socioeconomic characteristics were collected, including gender (male or female), age, marital status (single or married), education level (≤ high school, college, or > college), and residence (urban or rural). Additionally, lifestyle habits and comorbidity history were further collected, including smoking status (current smoker, former smoker, or non-smoker), alcohol consumption (non-drinker, former drinker, or drinker), history of cancer, Chronic kidney disease (CKD), CVD, hypertension, and diabetes (yes or no). Additionally, physical examinations and lab tests, including blood pressure (BP), weight, height, total cholesterol (TC), low-density LDL, uric acid (UA), HDL levels, triglycerides (TG), and fasting blood glucose (FBG), high-sensitivity C-reactive protein (hs-CRP), Blood Urea Nitrogen (BUN), WC, HbA1c, and lipid profiles, were considered as potential confounding variables. The participant's blood pressure was documented as the average of three readings taken while seated after a 5-min rest. Weight, height, and waist circumference were measured with participants dressed in light clothing and without shoes. At baseline, trained personnel collected blood samples from CHARLS participants after an overnight fast. The samples were stored at −20 °C and transported to Beijing, where additional measurements were carried out following standard protocols.

Hypertension was defined as self-reported physician-diagnosed hypertension, the use of any antihypertensive medication, and BP ≥ 140/90 mmHg [27]. Hypertension was defined as either self-reported physician-diagnosed hypertension, the use of antihypertensive drugs, and a blood pressure reading of 140/90 mmHg or higher [28]. Chronic kidney disease was identified based on eGFR < 60 mL min-1/1.73m^2 [29] or a self-reported physician diagnosis: Have you been diagnosed with Kidney disease (except for tumor or cancer) by a doctor? Kidney function was evaluated by the estimated glomerular filtration rate(eGFR) using serum creatinine. The CKD-EPI creatinine equation was used to calculate eGFR [30]. Body mass index (BMI) was determined using the formula: BMI (kg/m^2) = weight/height^2. Depressive symptoms were evaluated through the 10-item version of the Center for Epidemiologic Studies Depression Scale (CES-D). Participants with a CES-D score of 10 or above were classified as having depressive symptoms [31].

Ascertainment of outcomes

The primary outcome of this study is the incidence of new-onset cardiovascular disease, with secondary outcomes including the occurrence of new-onset stroke and cardiac events. In line with established precedents [32], the diagnosis of new-onset CVD was made when new-onset stroke or cardiac events were identified. New-onset stroke and cardiac events were assessed through the following questions: "Have you been diagnosed with a stroke by a doctor?"; "Since the last follow-up visit, have you been diagnosed with a stroke by a doctor?"; "Compared to the last time we interviewed you, has your stroke condition improved, stayed the same, or worsened?" The timing of stroke events was determined by participants' responses to the following questions: "When was the first time you were diagnosed with a stroke?"; "When was your most recent stroke?" The assessment of new-onset cardiac events was conducted similarly to that of new-onset stroke. Participants were followed up in four waves of interviews from 2011 until the onset of CVD or up to 2018, whichever occurred first [33].

Statistical analysis

All statistical analyses were performed using RStudio version 4.3.3. A two-tailed P-value of less than 0.05 was deemed statistically significant. Continuous variables were expressed as either mean ± standard deviation (SD) or median with interquartile range, depending on the data distribution. Baseline comparisons were made using analysis of variance (ANOVA) for normally distributed variables and the Kruskal–Wallis H test for non-normally distributed variables. Categorical data were presented as counts and percentages, with differences assessed using the chi-square test. A trend test was carried out using the median of each eGDR quartile. Kaplan–Meier curves were used to depict the cumulative incidence of CVD, with differences compared via the log-rank test. The incidence rate of CVD events was reported per 1000 person-years. Three Cox proportional hazard models were employed to estimate hazard ratios (HR) between eGDR and CVD, along with corresponding 95% confidence intervals (CI). The proportional hazards assumption for each variable in the model was tested using the Schoenfeld residuals test, and no violations were found. Collinearity among continuous variables was assessed using the variance inflation factor (VIF) before Cox regression analysis. Model 1 was unadjusted; Model 2 included adjustments for age, gender, rural residence, marital status, education level, and smoking and drinking status; and Model 3 was further adjusted for HDL, BUN, UA, high-sensitivity hsCRP, and chronic kidney disease

(Participants were also stratified based on the presence of MetS or CircS. To explore the dose–response relationship between eGDR and CVD incidence, restricted cubic splines (RCS) were used within the Cox regression model, adjusting for covariates in Model 3. Receiver operating characteristic (ROC) curves were generated to evaluate the predictive value of eGDR for CVD incidence, and a calibration curve was created to assess model accuracy. Furthermore, decision curve analysis (DCA) was conducted to estimate the clinical utility of the model. Subgroup analysis examined differences in CVD incidence across various eGDR subgroups. Sensitivity analysis was performed by redefining hypertension (130/80 mm Hg) in the eGDR calculation to assess the robustness of the main findings.

Results

Baseline characteristics

Baseline characteristics stratified by eGDR quartiles are shown in Table 1 (Q1: 6.29 [5.76, 6.71]; Q2: 7.91 [7.49, 8.49]; Q3: 10.47 [10.08, 10.77]; Q4: 11.58 [11.30, 11.95]). A total of 6,507 participants were included in this study, with a median age of 58.00 [52.00, 64.00] years, and 55% were female. Compared with the lowest quartile (Q1), participants in the higher quartiles (Q2-Q4) were younger on average. They had lower systolic and diastolic blood pressure, body mass index (BMI), waist circumference, HbA1c, TC, LDL), UA, hs-CRP, and HDL levels, as well as blood pressure, TG, and FBG, with lower rates of obesity (all $P < 0.001$). Meanwhile, participants in the lower eGDR quartiles had a higher prevalence of hypertension, diabetes, heart disease, stroke, and depression. Notably, individuals with higher eGDR were more likely to be married, have higher educational attainment, and tend to live in rural areas, with the highest rates of smoking (40.7%) and alcohol consumption (40.0%). Additionally, there were no significant differences in BUN and kidney disease across the quartiles. The baseline characteristics of individuals included in the CVD analysis are as follows (Supplementary File 1, Table S1).

Associations of baseline eGDR with incident CVD

Over a median follow-up period of 87 months, 679 first CVD events (10.4%) were recorded, including heart disease and stroke. The incidence rates of CVD among Q1-Q4 participants were 15, 11, 8.3, and 7.3 per 1000 person-years, respectively. The dose–response curve between eGDR and CVD is illustrated in Fig. 1. Across different metabolic and circadian rhythm subgroups, and irrespective of covariate adjustments, the multivariable-adjusted restricted cubic spline analysis also revealed a significant dose–response relationship between eGDR and the incidence of first CVD (all $P < 0.001$, P for non-linearity > 0.05). Kaplan–Meier cumulative incidence curve analysis indicated that from Q1 to Q4 groups, individuals with higher eGDR had lower cumulative incidences of first CVD(Supplementary File 1, Fig. 2), with statistically significant differences observed across different metabolic and circadian rhythm subgroups (log-rank test $P < 0.001$)(Fig. 2, Supplementary File 1, Fig. 3). The Cox proportional hazards model confirmed a significant association between baseline eGDR levels and the incidence of first CVD, first heart disease, and first stroke. After adjusting for potential confounders, in Model 3, each 1.0-SD increase in eGDR was associated with a 7% reduction in CVD risk [HR 0.93 (95% CI 0.89, 0.97)], a 12% reduction in stroke risk (HR 0.88 [95% CI 0.83, 0.94]), and a 6% reduction in heart disease risk [HR 0.94 [95% CI 0.89, 1.00)](Table 2).

The relationship between eGDR and CVD risk under different metabolic and circadian rhythm conditions

Throughout the follow-up period, we tracked new-onset CVD events among the participants. Among the 2,470 participants with MetS, 361 cases (14.6%) experienced their first CVD event, while 318 cases (7.88%) were recorded among the 4,037 non-MetS participants. Similarly, among the 2,882 participants with circadian rhythm disturbances (CircS), 329 cases (11.4%) experienced their first CVD event, whereas 350 cases (9.66%) were observed among the 3,625 non-CircS participants. Further analysis revealed that the incidence rates of first coronary heart disease (CHD) and first stroke in the MetS and CircS groups were 8.22%, 7.21%, and 5.18%, 3.12%, respectively, while the rates in the non-MetS and non-CircS groups were 7.88%, 5.07%, and 5.21%, 4.25%, respectively. As shown in Table 3, compared to the lowest eGDR quartile (Q1), the other eGDR groups were significantly associated with a reduced incidence of first CVD in the MetS, non-MetS, CircS, and non-CircS groups in Model 3. Specifically, in the MetS group, the HRs (95% CI) for the first CVD in Q2, Q3, and Q4 were 0.78 (0.61, 1.01), 0.52 (0.38, 0.73), and 0.73 (0.45, 1.17), respectively, with a trend test P-value of 0.007. In the non-MetS group, the corresponding HRs (95% CI) were 0.76 (0.51, 1.15), 0.67 (0.44, 1.01), and 0.51 (0.34, 0.76), with a trend test P-value of 0.001. In the non-CircS group, the corresponding HRs (95% CI) were 0.74 (0.53, 1.04), 0.69 (0.50, 0.96), and 0.55 (0.39, 0.76), with a trend test P-value of 0.001. In the CircS group, the corresponding HRs (95% CI) were 0.85 (0.66, 1.10), 0.54 (0.38, 0.76), and 0.69 (0.42, 1.13), with a trend test P-value of 0.022. Furthermore, in the CircS group, higher eGDR levels were associated with a 12% reduction in CVD risk compared to a 7% reduction in the non-CircS

Table 1 Baseline characteristics of participants stratified by quartiles of estimated glucose disposal rate

Characteristic	Overall N = 6,507	Quartiles of eGDR				p-value
		Q1 N = 1,627	Q2 N = 1,627	Q3 N = 1,629	Q4 N = 1,624	
Gender, n (%)						0.015
Female	3,564 (55)	935 (57)	875 (54)	907 (56)	847 (52)	
Male	2,943 (45)	692 (43)	752 (46)	722 (44)	777 (48)	
Age,years	58.00 (52.00,64.00)	60.00 (54.00,66.00)	60.00 (54.00,66.00)	56.00 (49.00,62.00)	57.00 (50.00,63.00)	< 0.001
Marital, n (%)	5,817 (89)	1,447 (89)	1,388 (85)	1,505 (92)	1,477 (91)	< 0.001
Local, n (%)						< 0.001
City	2,229 (34)	678 (42)	516 (32)	553 (34)	482 (30)	
Rural	4,278 (66)	949 (58)	1,111 (68)	1,076 (66)	1,142 (70)	
Education, n (%)						< 0.001
Elementary school and below	4,528 (70)	1,133 (70)	1,213 (75)	1,069 (66)	1,113 (69)	
Junior high school	1,314 (20)	320 (20)	288 (18)	382 (23)	324 (20)	
High school and above	665 (10)	174 (11)	126 (7.7)	178 (11)	187 (12)	
Hypertension, n (%)	2,995 (46)	1,622 (100)	1,317 (81)	9 (0.6)	47 (2.9)	< 0.001
Diabetes, n (%)	956 (15)	429 (26)	246 (15)	181 (11)	100 (6.2)	< 0.001
Chronic kidney disease, n (%)	1,344 (21)	356 (22)	373 (23)	321 (20)	294 (18)	0.003
CES-D, scoring	7.00 (3.00, 12.00)	7.00 (3.00, 12.00)	7.00 (3.00, 13.00)	7.00 (3.00, 12.00)	8.00 (3.00, 12.00)	0.033
Sleep time, hours	6.00 (5.00, 8.00)	7.00 (5.00, 8.00)	6.00 (5.00, 8.00)	7.00 (5.00, 8.00)	6.75 (5.00, 8.00)	0.052
Drinking, n (%)						< 0.001
Never	3,984 (61)	1,004 (62)	973 (60)	1,020 (63)	987 (61)	
Former	512 (7.9)	170 (10)	140 (8.6)	94 (5.8)	108 (6.7)	
Current	2,011 (31)	453 (28)	514 (32)	515 (32)	529 (33)	
Smoking, n (%)						< 0.001
Never	4,035 (62)	1,068 (66)	960 (59)	1,051 (65)	956 (59)	
Former	521 (8.0)	169 (10)	124 (7.6)	135 (8.3)	93 (5.7)	
Current	1,951 (30)	390 (24)	543 (33)	443 (27)	575 (35)	
SBP, mmHg	125.00 (113.00, 140.00)	142.00 (132.00, 153.50)	137.00 (125.00, 149.50)	116.50 (109.00, 124.00)	113.50 (106.00, 121.75)	< 0.001
DBP, mmHg	74.00 (66.50, 82.50)	83.00 (74.50, 90.00)	79.00 (72.00, 87.00)	70.00 (64.50, 76.00)	67.50 (62.00, 73.50)	< 0.001
Waist,cm	84.50 (77.80, 92.00)	94.20 (90.00, 99.10)	81.50 (76.40, 87.00)	87.00 (84.00, 91.00)	75.20 (71.20, 78.35)	< 0.001
BMI, kg/m^2	23.22 (20.96, 25.88)	26.31 (24.31, 28.57)	22.28 (20.32, 24.66)	24.01 (22.43, 25.63)	20.70 (19.25, 22.17)	< 0.001
BUN, mg/dL	15.07 (12.55, 18.15)	15.04 (12.72, 18.12)	15.27 (12.52, 18.35)	15.04 (12.44, 18.07)	14.99 (12.46, 17.95)	0.47
FBG, mg/dL	102.06 (94.50, 111.96)	106.74 (98.46, 120.24)	102.42 (95.22, 112.14)	101.52 (94.32, 109.98)	98.37 (91.80, 106.38)	< 0.001
TC, mg/dL	191.37 (168.17, 216.11)	199.49 (175.90, 225.39)	190.98 (168.94, 214.56)	190.59 (168.17, 214.95)	184.41 (161.99, 208.18)	< 0.001
TG, mg/dL	103.54 (74.34, 150.45)	130.98 (92.93, 191.16)	101.78 (74.34, 148.68)	103.54 (73.46, 144.26)	85.85 (63.72, 120.36)	< 0.001
HDL, mg/dL	49.48 (40.98, 59.92)	44.85 (37.50, 53.35)	51.42 (41.75, 61.47)	49.10 (40.59, 58.76)	54.51 (45.23, 64.56)	< 0.001
LDL, mg/dL	115.59 (94.72, 138.40)	121.78 (99.36, 145.36)	114.05 (93.17, 135.70)	117.14 (96.26, 138.79)	110.18 (91.24, 132.22)	< 0.001
hs-CRP, mg/L	0.99 (0.53, 2.04)	1.46 (0.79, 2.84)	0.96 (0.51, 1.95)	0.92 (0.54, 1.78)	0.72 (0.42, 1.47)	< 0.001
HbA1c, %	5.20 (4.90, 5.40)	5.30 (5.00, 5.70)	5.10 (4.80, 5.40)	5.20 (4.90, 5.40)	5.00 (4.80, 5.30)	< 0.001
UA, mg/dL	4.25 (3.54, 5.08)	4.56 (3.78, 5.42)	4.28 (3.55, 5.09)	4.18 (3.53, 5.00)	4.02 (3.39, 4.78)	< 0.001
eGDR	9.48 (7.08, 11.04)	6.29 (5.76, 6.71)	7.91 (7.49, 8.49)	10.47 (10.08, 10.77)	11.58 (11.30, 11.95)	< 0.001
Elevated waist circumference, n (%)	3,809 (59)	1,601 (98)	764 (47)	1,304 (80)	140 (8.6)	< 0.001
Elevated serum triglycerides, n (%)	1,637 (25)	654 (40)	400 (25)	363 (22)	220 (14)	< 0.001
Reduced serum HDL-C, n (%)	2,508 (39)	877 (54)	577 (35)	655 (40)	399 (25)	< 0.001

Table 1 (continued)

Characteristic	Overall N = 6,507	Quartiles of eGDR				p-value
		Q1 N = 1,627	Q2 N = 1,627	Q3 N = 1,629	Q4 N = 1,624	
Elevated blood pressure, n (%)	3,342 (51)	1,624 (100)	1,367 (84)	183 (11)	168 (10)	< 0.001
Elevated plasma glucose, n (%)	3,780 (58)	1,160 (71)	968 (59)	908 (56)	744 (46)	< 0.001
Short sleep, n (%)	1,889 (29)	423 (26)	504 (31)	472 (29)	490 (30)	0.010
Depression, n (%)	2,390 (37)	567 (35)	628 (39)	574 (35)	621 (38)	0.044
Metabolic syndrome, n (%)	2,801 (43)	1,397 (86)	730 (45)	531 (33)	143 (8.8)	< 0.001
Circadian syndrome, n (%)	2,384 (37)	1,154 (71)	628 (39)	476 (29)	126 (7.8)	< 0.001
Heart Disease, n (%)	416 (6.4)	124 (7.6)	118 (7.3)	96 (5.9)	78 (4.8)	0.003
Stroke, n (%)	304 (4.7)	136 (8.4)	79 (4.9)	47 (2.9)	42 (2.6)	< 0.001
Cardiovascular diseases, n (%)	679 (10)	244 (25)	182 (11)	135 (8)	118 (7)	< 0.001

BMI body mass index, *BUN* blood urea nitrogen, *DBP* diastolic blood pressure, *DM* diabetes mellitus, *eGDR* estimated glucose disposal rate, *FBG* fasting blood glucose, *HbA1c* glycosylated hemoglobin A1c, *HDL* high density lipoprotein, *hsCRP* high-sensitivity C-reactive protein, *LDL* low density lipoprotein, *SBP* systolic blood pressure, *TC* total cholesterol, *TG* triglycerides, *UA* uric acid, *WC* waist circumference

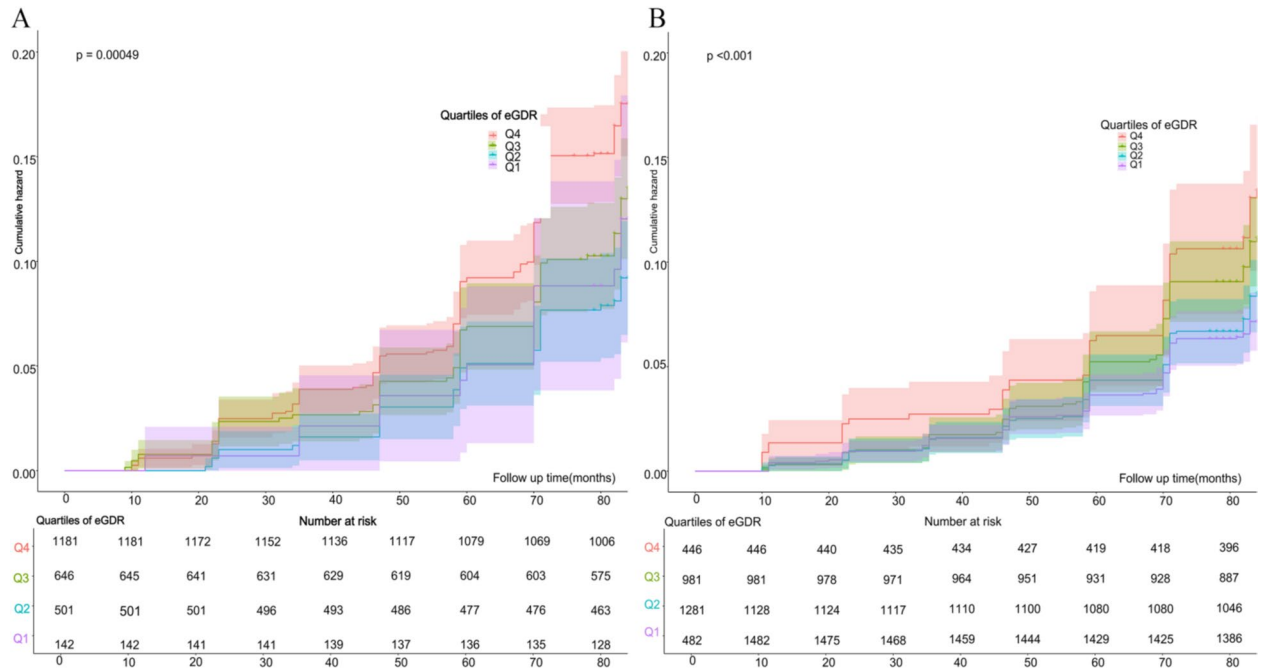

Fig. 2 The Kaplan–Meier analysis for CVD was based on eGDR quartiles for CircS participants (**A**), participants with No-CircS(**B**)

group. Similarly, in the MetS group, the predictive effect of eGDR was slightly more substantial (12% risk reduction) compared to a 9% risk reduction in the non-MetS group. Similar results were observed in the eGDR models predicting the first stroke across the MetS, non-MetS, CircS, and non-CiscS groups (Supplementary File 1, Table S2). However, in the models predicting the first CHD events based on eGDR, the results were not significant ($p > 0.05$) (Supplementary File 1, Table S3).

Mediation analyses

In the mediation analysis of this study, we found that CircS significantly mediated the relationship between eGDR and new-onset CVD events. In the

Table 2 Multivariate-adjusted hazard ratios (95% confidence intervals) of estimated glucose disposal rate for cardiovascular diseases

Characteristic	CVD			Stroke			CHD		
	HR (95% CI)	p-value	P for trend	HR (95% CI)	p-value	P for trend	HR (95% CI)	p-value	P for trend
Model1									
eGDR	0.88 (0.85, 0.91)	< 0.001	< 0.001	0.81 (0.77, 0.85)	< 0.001	< 0.001	0.93 (0.89, 0.97)	< 0.001	< 0.001
eGDR4									
Q1	Ref			Ref			Ref		
Q2	0.73 (0.60, 0.88)	0.001		0.57 (0.43, 0.75)	< 0.001		0.95 (0.74, 1.22)	0.672	
Q3	0.53 (0.43, 0.65)	< 0.001		0.33 (0.24, 0.47)	< 0.001		0.76 (0.58, 0.99)	0.043	
Q4	0.46 (0.37, 0.58)	< 0.001		0.30 (0.21, 0.42)	< 0.001		0.62 (0.46, 0.82)	< 0.001	
Model2									
eGDR	0.89 (0.86, 0.92)	< 0.001	< 0.001	0.94 (0.90, 0.98)	0.004	< 0.001	0.82 (0.78, 0.86)	< 0.001	< 0.001
eGDR4									
Q1	Ref			Ref			Ref		
Q2	0.76 (0.62, 0.92)	0.005		0.96 (0.75, 1.24)	0.778		0.60 (0.45, 0.79)	< 0.001	
Q3	0.59 (0.48, 0.73)	< 0.001		0.81 (0.62, 1.06)	0.132		0.39 (0.28, 0.55)	< 0.001	
Q4	0.50 (0.40, 0.63)	< 0.001		0.67 (0.50, 0.89)	0.005		0.32 (0.22, 0.46)	< 0.001	
Model3									
eGDR	0.89 (0.86, 0.92)	< 0.001	< 0.001	0.93 (0.89, 0.98)	0.003	0.0011	0.82 (0.78, 0.87)	< 0.001	< 0.001
eGDR4									
Q1	Ref			Ref			Ref		
Q2	0.76 (0.62, 0.93)	0.007		0.95 (0.73, 1.23)	0.698		0.62 (0.47, 0.82)	< 0.001	
Q3	0.59 (0.48, 0.73)	< 0.001		0.80 (0.61, 1.05)	0.113		0.40 (0.29, 0.56)	< 0.001	
Q4	0.50 (0.40, 0.63)	< 0.001		0.65 (0.48, 0.87)	0.004		0.33 (0.23, 0.48)	< 0.001	

Model 1: unadjusted

Model 2: adjusted for age, sex, local, marital, education, smoking, and drinking

Model 3: model 2 + further adjusted for HDL, BUN, UA, hsCRP, Chronic kidney disease, *BUN* blood urea nitrogen, *CI* confidence interval, *eGDR* estimated glucose disposal rate, *HDL* high density lipoprotein, *HR* hazard ratio, *hsCRP* high-sensitivity C-reactive protein, *LDL* low density lipoprotein, Ref reference, *TC* total cholesterol, *TG* triglyceride, *UA* uric acid alncident rate was presented as per 1000 person-years of follow-up (TG,LDL,TC, and eGDR all exhibit multicollinearity, hence they are not included)

unadjusted model, CircS accounted for 18.03% of the association between eGDR and new-onset CVD events; this proportion slightly increased to 19.53% in the model adjusted for all covariates (Supplementary File 1, Figure S4). Further exploration of CircS as a mediator in the relationship between eGDR and new-onset CHD and stroke events revealed that CircS did not achieve statistical significance as a mediator in either the unadjusted or covariate-adjusted models (Supplementary File 1, Figure S5- S6). MetS also did not exhibit a significant mediating effect in the association between eGDR and new-onset CHD and stroke events (Supplementary File 1, Figure S7-S9).

Subgroup analysis

In this study, we conducted extensive subgroup analyses to explore the association between eGDR and CVD risk across different subgroups. The analysis considered several factors, including sex, age, marital status, BMI, CircS, MetS, increased waist circumference, elevated serum triglycerides, reduced serum HDL-C, elevated blood pressure, elevated plasma glucose, short sleep duration, and depression. The study results showed a significant negative correlation between eGDR and CVD risk in most subgroups. However, statistical significance was not achieved in the subgroups of marital status and BMI ≥ 24 kg/m^2 ($p > 0.05$). In contrast, the relationship between eGDR and CVD incidence was consistent with the overall analysis results in most other subgroups. Notably, eGDR showed variability in predicting CVD risk across different BMI subgroups. Specifically, the subset with a BMI between 18.5 and 24 kg/m^2 demonstrated a stronger association between eGDR and CVD risk [HR: 0.90, 95% CI 0.86–0.93], and this difference was statistically significant in the adjusted model (P for interaction = 0.025). Additionally, there was some variation across age groups (P for interaction = 0.045). However, apart from the BMI and age subgroups, there were no significant interactions in other subgroups (Fig. 3).

Table 3 Analysis of the relationship between eGDR and CVD risk based on metabolic and circadian rhythm states

Characteristic	Event, n(%)	Model1		Model2		Model3	
MetS		**HR (95% CI)[1]**	**p-value**	**HR (95% CI)[1]**	**p-value**	**HR (95% CI)[1]**	**p-value**
eGDR	361 (5.55%)	0.88 (0.83,0.92)	< 0.001	0.88 (0.83, 0.93)	< 0.001	0.88 (0.83, 0.93)	< 0.001
eGDR4							
Q1	208 (57.6%)	Ref		Ref		Ref	
Q2	91 (25.2%)	0.78 (0.61,1.00)	0.052	0.78 (0.61, 1.00)	0.05	0.78 (0.61, 1.01)	0.055
Q3	43 (11.9%)	0.50 (0.36, 0.70)	< 0.001	0.53 (0.38, 0.73)	< 0.001	0.52 (0.38, 0.73)	< 0.001
Q4	19 (5.3%)	0.74 (0.46, 1.18)	0.199	0.75 (0.47, 1.20)	0.228	0.73 (0.45, 1.17)	0.187
P for trend			< 0.001		0.00361		0.007
No-MetS							
eGDR	318 (4.89%)	0.90 (0.85, 0.96)	< 0.001	0.91 (0.86, 0.97)	0.002	0.91 (0.86, 0.97)	0.003
Egdr (Q1)	31 (9.7%)	Ref		Ref		Ref	
Q2	92 (28.9%)	0.77 (0.51, 1.16)	0.209	0.77 (0.51, 1.16)	0.211	0.76 (0.51, 1.15)	0.195
Q3	95 (29.9%)	0.62 (0.42, 0.94)	0.023	0.66 (0.44, 1.00)	0.05	0.67 (0.44, 1.01)	0.053
Q4	100 (31.4%)	0.48 (0.32, 0.72)	< 0.001	0.51 (0.34, 0.76)	< 0.001	0.51 (0.34, 0.76)	0.001
P for trend			< 0.001		< 0.001		< 0.001
No-CircS							
eGDR	350 (5.38%)	0.91 (0.87, 0.96)	< 0.001	0.92 (0.88, 0.97)	0.003	0.93 (0.88, 0.98)	0.003
eGDR4							
Q1	57 (16.3%)	Ref		Ref		Ref	
Q2	94 (26.9%)	0.74 (0.53, 1.03)	0.077	0.74 (0.53, 1.04)	0.08	0.74 (0.53, 1.04)	0.08
Q3	97 (27.7%)	0.64 (0.46, 0.88)	0.007	0.68 (0.49, 0.95)	0.024	0.69 (0.50, 0.96)	0.029
Q4	102 (29.1%)	0.52 (0.37, 0.72)	< 0.001	0.55 (0.39, 0.76)	< 0.001	0.55 (0.39, 0.76)	< 0.001
P for trend			< 0.001		< 0.001		< 0.001
CircS							
eGDR	329 (5.06%)	0.89 (0.84, 0.94)	< 0.001	0.89 (0.84, 0.94)	< 0.001	0.88 (0.83, 0.93)	< 0.001
eGDR4							
Q1	182 (55.3%)	Ref		Ref		Ref	
Q2	89 (27.1%)	0.87 (0.67, 1.12)	0.266	0.86 (0.66, 1.11)	0.242	0.85 (0.66, 1.10)	0.224
Q3	41 (12.5%)	0.54 (0.38, 0.75)	< 0.001	0.54 (0.39, 0.77)	< 0.001	0.54 (0.38, 0.76)	< 0.001
Q4	17 (5.2%)	0.71 (0.43, 1.16)	0.173	0.70 (0.42, 1.15)	0.161	0.69 (0.42, 1.13)	0.142
P for trend			< 0.001		0.00772		0.0224

Model 1: unadjusted

Model 2: adjusted for age, sex, local, marital, education, smoking, and alcohol

Model 3:model 2 + further adjusted for HDL,BUN, UA, hsCRP, Chronic kidney disease, *MetS* Metabolic Syndrome group, *NO-MetS* Non-Metabolic Syndrome group, *CircS* Circadian Rhythm Syndrome group, *No-CircS* Non-Circadian Rhythm Syndrome group. *Ref* reference, *BUN* blood urea nitrogen, *CI* confidence interval, *eGDR* estimated glucose disposal rate, *HDL* high density lipoprotein, *HR* hazard ratio, *hsCRP* high-sensitivity C-reactive protein, *LDL* low density lipoprotein, *Ref* reference, *TC* total cholesterol, *TG* triglyceride, *UA* uric acid aIncident rate was presented as per 1000 person-years of follow-up (TG,LDL,TC, and eGDR all exhibit multicollinearity, hence they are not included)

Sensitivity analyses

In the sensitivity analysis, when only individuals with normal glycemic status were included, the results did not change substantially (Supplementary File 1, Table S4). Similar results were observed when we recalculated eGDR using the redefined hypertension criteria (≥ 130/80 mm Hg).

Predictive performance of eGDR in the incident CVD

In this study, we plotted time-dependent ROC curves based on Model 3 to assess the predictive performance for CVD, CHD, and stroke risks at different follow-up time points (1 year, 3 years, 5 years, 7 years). As shown in Fig. 4, at the 1-year follow-up, the predictive model for CVD events showed an AUC value of 0.615 (95%

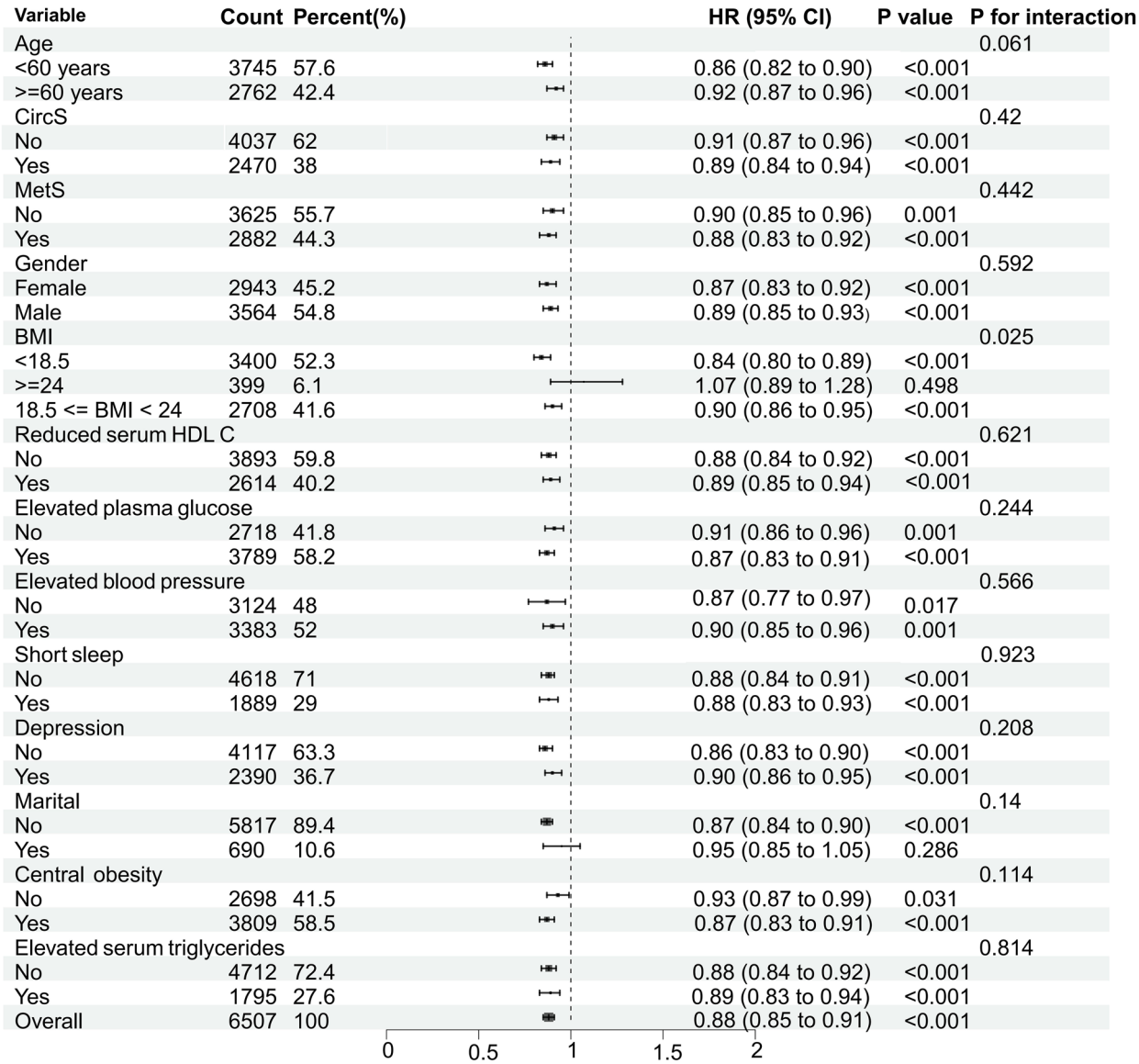

Fig. 3 Subgroup and interaction analyses among the quartile 1 – 4 and CVD across various subgroups

CI 0.511–0.720), whereas the stroke predictive model exhibited a higher AUC value of 0.745 (95% CI 0.656–0.835). Moreover, we observed that the predictive performance for CVD gradually improved with increasing follow-up time. Additionally, the calibration curves for the CVD and stroke predictive models were highly consistent with actual observations (Fig. 5), validating the match between predicted values and actual occurrence probabilities. Furthermore, decision curve analysis indicated that at the thresholds corresponding to a 9–24% incidence rate for CVD and a 3–15% incidence rate for stroke, our decision curves were above the "no intervention" and "all intervention" lines (Supplementary File Figure S10). However, it is noteworthy that compared to the CVD and stroke predictive models, the performance of the CHD model was suboptimal, with consistently lower AUC values.

Discussion

In our study, we were the first to confirm the predictive value of eGDR for CVD risk in populations with different metabolic and circadian rhythm profiles. The main conclusions are as follows: (1) eGDR has been demonstrated to be an independent predictor of CVD risk, with lower eGDR levels significantly associated with higher cardiovascular disease risk (including heart

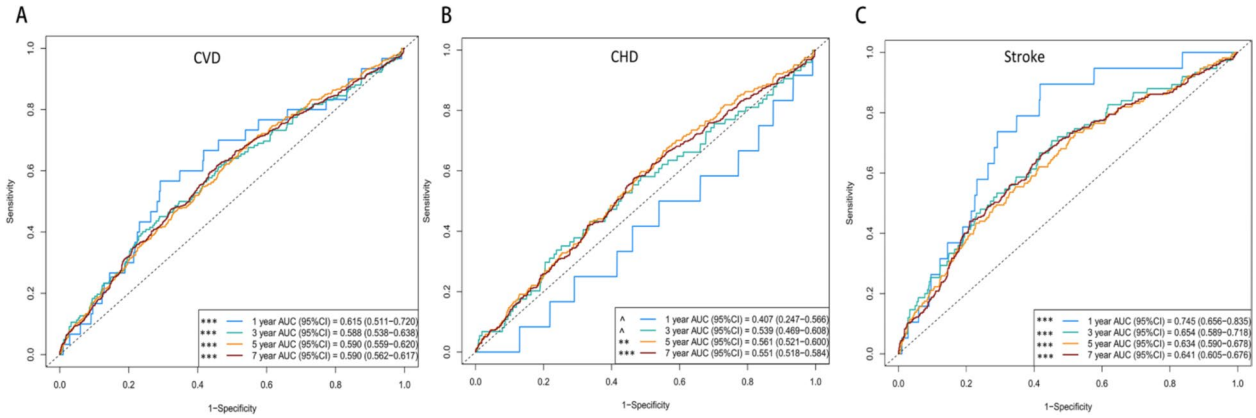

Fig. 4 The receiver operating characteristic curves of the eGDR as an IR marker to predict MACCEs (**A**-CVD, **B**-CHD,**C**-Stroke). The basic model adjusted age, gender, marital, education, smoking, drinking, local, HDL, BUN, UA, hsCRP, chronic kidney disease

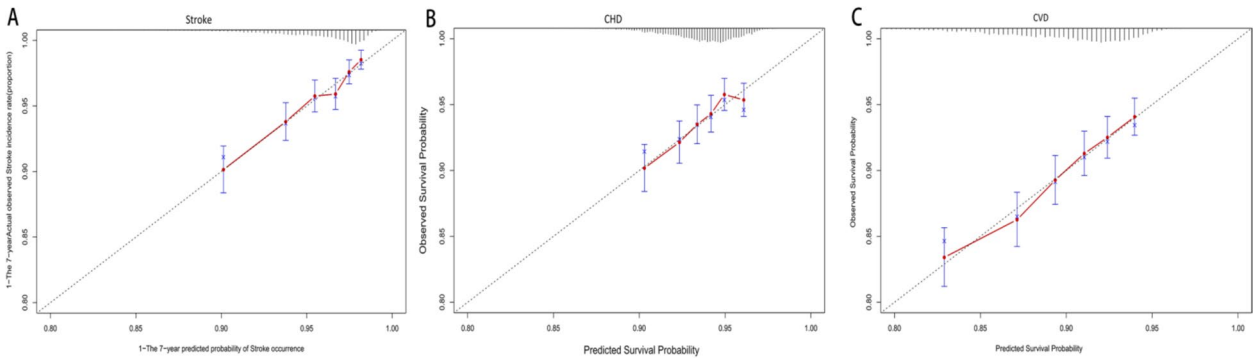

Fig. 5 Based on Model 3, the calibration curves for 87-month CVD (**A**), CHD (**B**), and Stroke (**C**) event survival are presented. The dashed line represents an excellent match between the nomogram prediction (X-axis) and the actual survival outcome (Y-axis). The closer the points are to the dashed line, the higher the prediction accuracy

disease and stroke), particularly in groups with MetS or CircS, where the association between reduced eGDR levels and increased risk is more pronounced. (2) The correlation between eGDR and CVD risk shows a linear trend, and this relationship is unaffected by factors such as age, gender, smoking, or alcohol consumption. (3) CircS partially mediates the relationship between eGDR and CVD risk. (4) The results of the ROC curve and calibration curve indicate that the predictive model has good performance and accuracy. In summary, our study findings reinforce the hypothesis that eGDR is a crucial predictor of CVD and underscore its potential as a target for preventing CVD in individuals with metabolic and circadian rhythm disturbances. This offers a novel perspective for future research and clinical interventions.

In light of human circadian clock disruption, circadian rhythm disorders have become a significant phenomenon of widespread concern [34]. Circadian rhythm disorders are misaligned between the central circadian pacemaker and the 24-hour behavioral rhythms, influenced by light exposure, feeding, and fasting cycles [35]. Disruptions in circadian rhythm can affect glucose metabolism by modulating the secretion of various hormones, including insulin, glucocorticoids, growth hormone (GH), thyroid hormones, and melatonin [36]. Consequently, such disruptions may result in glucose metabolism dysfunctions. In a randomized crossover study, Morris et al. found that circadian rhythm disorders can lead to decreased glucose tolerance [35, 37–43], thereby increasing the risk of diabetes. Studies on animal models have further validated the strong connection between circadian rhythm disruptions and metabolic disorders. Turek et al. discovered that in the early stages of circadian rhythm disruption, mice displayed swallowing difficulties along with symptoms of MetS, such as hyperlipidemia, hyperglycemia, and hypoinsulinemia [44, 45]. These findings reveal the potential negative impacts of circadian rhythm disruptions on metabolic health. In

an adult cohort study, it was found that individuals with shorter sleep durations are more prone to MetS-related mortality risks and are more likely to develop central autonomic and metabolic dysfunctions compared to those with average sleep durations [44]. These findings further emphasize the close relationship between circadian rhythms and MetS. Several aspects of modern life, such as widespread artificial lighting, regulated indoor temperatures, continuous food availability, shift work, and frequent travel across time zones, can disrupt circadian rhythms. These factors are closely related to the components of MetS and CircS and the occurrence of CVD [46, 47]. Moreover, research indicates a potential causal relationship between circadian rhythm disruptions and IR, which is closely tied to the development of type 2 diabetes and CVD [48, 49]. Recent research has also found that the coexistence of IR and MetS significantly raises the risk of developing diabetes or CVD, thus making the accurate assessment of IR more effective in identifying CVD risk in MetS patients [50, 51]. In conclusion, metabolic and circadian rhythm disruptions are closely related to CVD risk, and such disruptions may exacerbate insulin resistance, further elevating the risk of developing CVD.

IR plays a significant role as a potential mechanism for increased CVD risk by leading to chronic inflammation, oxidative stress, and endothelial dysfunction by activating inflammation-related genes and disrupting insulin signaling, thereby damaging vascular health and promoting CVD. Earlier research has demonstrated a strong link between insulin resistance and conditions like diabetes, lipid metabolism disorders, and hypertension, all of which are significant risk factors for cardiovascular events [50]. Thus, in assessing chronic vascular complications and mortality in both the general population and patients with specific conditions, the evaluation of insulin resistance has emerged as an essential and additional risk factor for cardiovascular disease. Since traditional IR assessment methods are typically invasive and expensive, eGDR presents a more convenient and economical alternative. Moreover, a systematic review and meta-analysis of randomized controlled trials showed that sleep restriction decreases whole-body insulin sensitivity measured by the hyperinsulinemic-euglycemic clamp method, implying that sleep disturbances could negatively affect glucose metabolism [51]. Since sleep disturbances are generally regarded as a manifestation of circadian rhythm disruption, these findings underscore that eGDR shows excellent potential as a CVD risk assessment tool in populations with circadian rhythm disorders.

In a study of 191 type 1 diabetes (T1D) patients without a history of cardiovascular disease, eGDR was independently associated with the presence of two or more plaques ($P = 0.018$) and the maximum plaque height ($P < 0.01$). These findings indicate that eGDR may serve as a significant predictor of subclinical carotid atherosclerosis and cardiovascular risk [52]. Furthermore, Shi et al. [11]investigated the relationship between CircS and CVD, revealing that at baseline, the incidence of CKD in the CircS-only group was 25.3%, significantly higher than in the healthy group (13.5%), the MetS-only group (12.2%), and the group with both CircS and MetS (16.5%). Xiong et al. [53] reported similar findings, indicating that the CKD incidence rate in the CircS group was 5.03%, higher than in the healthy group (3.06%) and the MetS group (3.87%). Other studies have also indicated that participants with CircS have a significantly increased risk of developing CKD and a rapid decline in renal function compared to those without CircS [54]. Our study also found similar results using COX regression model analysis, with the CVD prevalence rate being 11.4% in the CircS group, higher than 9.66% in the non-CircS group, and the CVD prevalence rate being 14.6% in the MetS group, higher than 7.8% in the non-MetS group. These findings support the view that CircS and MetS are risk factors for CVD. In a UK study of 32 patients with type 1 diabetes, eGDR was found to be linked to an increased risk of thrombosis [55]. Xuan et al. [56]further validated the relationship between eGDR and ischemic heart disease, highlighting that eGDR could improve diagnostic accuracy for ischemic heart disease in the general population. Sun et al. [57] discovered a correlation between eGDR and arterial stiffness and found that it could predict long-term all-cause mortality. Mediation analysis revealed that arterial stiffness partially mediates the association between eGDR and mortality. Our study obtained similar results; after controlling for confounding factors, CircS partially mediated the relationship between eGDR and CVD, contributing 19.53%. Based on a review of published literature, eGDR has been proven to have considerable value in diagnosing and predicting CVD. Our findings are consistent with existing studies, particularly in populations with metabolic disorders and circadian rhythm disruptions, where eGDR shows excellent potential in predicting CVD events.

In this study, we found that higher eGDR levels were significantly correlated with a decreased risk of CVD incidence. The analysis of the clinical decision curve showed that, particularly within the threshold range of 8-24%, our model outperformed the 'Treat All' and 'Treat None' strategies. Moreover, our study found that among those diagnosed with CircS, high eGDR levels resulted in a 12% reduction in CVD risk, which was more pronounced than the 7% reduction in non-CircS

individuals. Similarly, when comparing MetS (12%) with the non-MetS group (9%), individuals in the MetS group exhibited a slightly more substantial risk reduction effect at high eGDR levels. In subgroup analysis, we found a significant interaction between eGDR, age, and BMI on CVD risk, consistent with previous studies. These findings suggested that eGDR could serve as a valuable marker for predicting CVD risk in MetS and CircS populations, with potential clinical applications, and we further expanded the existing literature by examining the role of eGDR in predicting CVD risk among individuals with metabolic disorders and circadian rhythm disruptions. Additionally, the research found that the relationship between eGDR levels and CVD risk might differ among various types of cardiovascular diseases. Furthermore, the findings suggest that CircS partially mediates this relationship. Previous studies [36] have established a causal link between insulin resistance and circadian rhythm disruptions, indicating that mitigating circadian rhythm disturbances could alleviate the adverse cardiovascular effects of IR. However, this relationship might be influenced by the overlap between components used to diagnose circadian rhythm disorders and those used in eGDR calculations. Therefore, carefully designed experimental studies and prospective clinical trials are needed to clarify the underlying biological mechanisms and provide more rigorous interpretations.

This study is based on data from the CHARLS, a large, nationally representative cohort study with a high response rate. The study effectively controlled for potential confounding factors through multivariable models. Our findings offer additional evidence supporting the clinical application of eGDR, suggesting that incorporating eGDR into routine practice could help healthcare professionals and patients recognize the significance of risk factors beyond blood glucose levels. However, several limitations should be considered. Firstly, there were significant differences in most baseline characteristics between the included and excluded groups, potentially reducing the results' reliability. As a result, our study may primarily suggest hypotheses for future research rather than definitive conclusions. Secondly, despite adjusting for many covariates in our model, residual confounding cannot be entirely ruled out, a common issue in observational studies. Thirdly, the endpoint events in this study were self-reported by participants based on a doctor's diagnosis, which may introduce recall bias and lead to inevitable misclassification [58]. However, this approach is widely accepted in cohort studies and has been shown to have minimal impact. Lastly, our study only included Chinese individuals aged 45 and above, which may limit the generalizability of our conclusions.

In summary, this study not only confirmed that low eGDR—a simple measure of insulin resistance—significantly increases the risk of incident CVD, stroke, and CHD events in the general Chinese population but also found that low eGDR is closely related to a higher risk of new-onset CVD events among populations with MetS and CircS. Additionally, the study found that eGDR has broad predictive ability for different types of cardiovascular diseases. Therefore, eGDR is expected to become an important predictive marker for the early identification of high-risk individuals for cardiovascular diseases, particularly in populations with metabolic and circadian rhythm disorders. In clinical practice, incorporating eGDR assessment into routine screenings for these high-risk populations could facilitate early intervention. Additionally, repeating this study in European populations and other demographic groups may yield similar results. Future research should continue to explore the interaction of eGDR with other cardiovascular risk factors and validate its predictive value in different races and populations.

Abbreviations

BMI	Body mass index
BP	Blood pressure
BUN	Blood urea nitrogen
CHARLS	China health and retirement longitudinal study
CI	Confidence interval
CVD	Cardiovascular diseases
eGDR	Estimated glucose disposal rate
FBG	Fasting blood glucose
HbA1c	Glycosylated hemoglobin A1c
HDL	High-density lipoprotein
HOMA-IR	Homeostasis model assessment for insulin resistance
HR	Hazard ratio
hsCRP	High-sensitivity C-reactive protein
LDL	Low-density lipoprotein
Q	Quartiles
RCS	Restricted cubic spline
TC	Total cholesterol
TG	Triglyceride
UA	Uric acid
WC	Waist circumference

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-024-01494-7.

Supplementary material 1.

Supplementary material 2.

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Author contributions

LC conceived and designed the experiments and wrote the manuscript. QY and WD organized the data and WZ performed the analyses.LJ and YS contributed to the quality control of the data and the finalization of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
CHARLS was approved by the Institutional Review Board of Peking University (approval number: IRB00001052-11015 for household survey and IRB00001052-11014 for blood sample), and all participants provided written consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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