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Relationship between stroke and estimated glucose disposal rate: results from two prospective cohort studies

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Abstract

Background Insulin resistance (IR) is a recognized contributor to stroke association, and the estimated glucose disposal rate (eGDR) is a dependable indicator of IR. However, the specific connections between eGDR, stroke prevalence, and overall mortality have not been thoroughly investigated. This study aimed to examine how eGDR correlates with stroke and overall death rate.

Methods The study leveraged information from the National Health and Nutrition Examination Survey (NHANES) spanning from 2007 to 2016. To unravel the data, the team utilized logistic regression, cox proportional hazards models, and restricted cubic splines (RCS) Sensitivity analyses excluded participants with a stroke history within the previous two years. Results were validated through analysis of the China Health and Retirement Longitudinal Study (CHARLS).

Results A higher eGDR is like a protective shield against strokes, with those in the top eGDR quartile exhibited a 60% reduction in stroke association (OR = 0.40, 95% CI, 0.22–0.73, $P = 0.003$). Additionally, a higher eGDR correlates with a lower overall death rate (HR = 0.71, 95% CI, 0.52–0.98, $P = 0.037$), particularly in individuals without a history of stroke. RCS analysis demonstrated that eGDR's influence on stroke association follows a non-linear pattern. Subgroup analysis revealed that the protective effect of eGDR was stronger in non-diabetic and non-hypertensive individuals.

Conclusion eGDR is inversely related to both stroke association and mortality, affirming its utility as a predictive marker of stroke.

Keywords Stroke, Estimated glucose disposal rate, Mortality, NHANES, CHARLS

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Introduction

A stroke is an acute cerebrovascular event caused by ischemic damage to brain tissue, typically resulting from either the obstruction or rupture of blood vessels. Strokes are generally classified into two categories: ischemic and hemorrhagic [1]. While extensively studied, the pathogenesis of stroke remains incompletely elucidated. Key risk factors include hypertension [2], hyperlipidemia [3], high body mass index (BMI) [4], as well as diabetes [5]. In addition to the above-mentioned risk factors for stroke, hypertrophic hypertensive cardiac disease with atrial fibrillation was the leading cardiac source of emboli in cardioembolic stroke, followed by isolated atrial fibrillation, rheumatic mitral valve disease, and systolic left ventricular dysfunction from both ischemic and non-ischemic causes [6].

The rise of these risk factors has surged as a result of socioeconomic development and lifestyle changes, particularly with respect to diabetes mellitus [7], hypertension, and hyperlipidemia [8]. Stroke has become the second leading cause of death globally, and although the incidence of stroke has declined in elderly people in the United States, it has increased in young people [9, 10].

Insulin resistance (IR) occurs when the body becomes less responsive to insulin, resulting in abnormalities in glucose and lipid metabolism [11]. Emerging evidence suggests a link between IR and increased stroke association, possibly through its contribution to atherosclerosis [12]. Furthermore, IR has been associated with hypertension, increased triglycerides, and decreased high-density lipoprotein (HDL), all of which are recognized as independent risk factors for adverse stroke outcomes. However, the exact mechanisms linking IR to these conditions remain poorly understood. Proposed explanations include metabolic dysfunction, endothelial cell impairment, oxidative stress, and heightened inflammatory activity [13–15]. Besides, IR plays a pivotal role in shaping the lipid triad, a trio of lipid abnormalities that are intricately connected to the onset of stroke and its associated risk factor conditions. This complicates the assessment of the independent effect of IR on stroke, underscoring the necessity for large-scale data analyses to minimize confounding variables [16–18].

The hyperinsulinemic-euglycemic clamp technique stands tall as the most accurate method for diagnosing IR, but its intricate procedures, hefty costs, and invasive approach make it less than ideal for everyday clinical practice [19]. To address these limitations, the estimated glucose disposal rate (eGDR) has emerged as a more straightforward alternative, particularly beneficial for those battling type 1 diabetes (T1D). This approach utilizes parameters such as hypertension status, waist circumference (WC), and glycosylated hemoglobin (HbA1c) [20]. The eGDR, based on these factors, offers a more straightforward and accurate assessment compared to several other methods and has been predominantly employed in large population-based cohort studies [21]. Previous research has identified an association between eGDR levels and both stroke and cardiovascular mortality, although these studies have primarily focused on diabetic populations. As a result, the potential confounding effects of diabetes on IR may have influenced the findings, complicating the assessment of IR's independent role [22–26]. To date, a comprehensive investigation of the direct connection between eGDR and stroke outcomes has not been conducted, thus this research seeks to bridge the gap.

Methods

Data source and participants

The study tapped into the treasure trove of data from the National Health and Nutrition Examination Survey (NHANES), diving deep into the nutritional well-being and health of individuals throughout the U.S. This program gathers a wide range of information, including demographic details, standardized questionnaires responses, physical examinations conducted at mobile screening units, and laboratory test results.

This research incorporated data from five biennial NHANES surveys conducted between 2007 to 2016. Initially, 23,427 participants were enrolled. Exclusion criteria were applied to individuals younger than 18 years ($n=715$), pregnant women ($n=257$), those with malignant tumors ($n=2,296$), and participants with missing data on HbA1c ($n=678$), other relevant variables ($n=576$), stroke diagnosis ($n=21$), or other cofactors. In the end, the final analysis comprised a total of 16,313 participants.

To validate the findings derived from NHANES, we drew upon foundational data from the China Health and Retirement Longitudinal Study (CHARLS), which was launched in 2011 and released on March 13, 2013. CHARLS 2011, a nationally representative survey, serves as a robust source of demographic, health, and socioeconomic data, complementing the NHANES dataset. The inclusion of CHARLS allowed for the cross-validation of our analyses and strengthened the reliability of our findings in a broader population context. This dataset represented an Eastern population sample, predominantly comprising individuals of Asian descent, with a focus on older adults, as over 98% of participants were aged 45 years or older. Initially, 10,131 individuals from CHARLS met the study criteria. Exclusion criteria were applied as follows: incomplete data on age, WC, or glycated hemoglobin ($n=205$); missing information on smoking history, gender, education level, or history

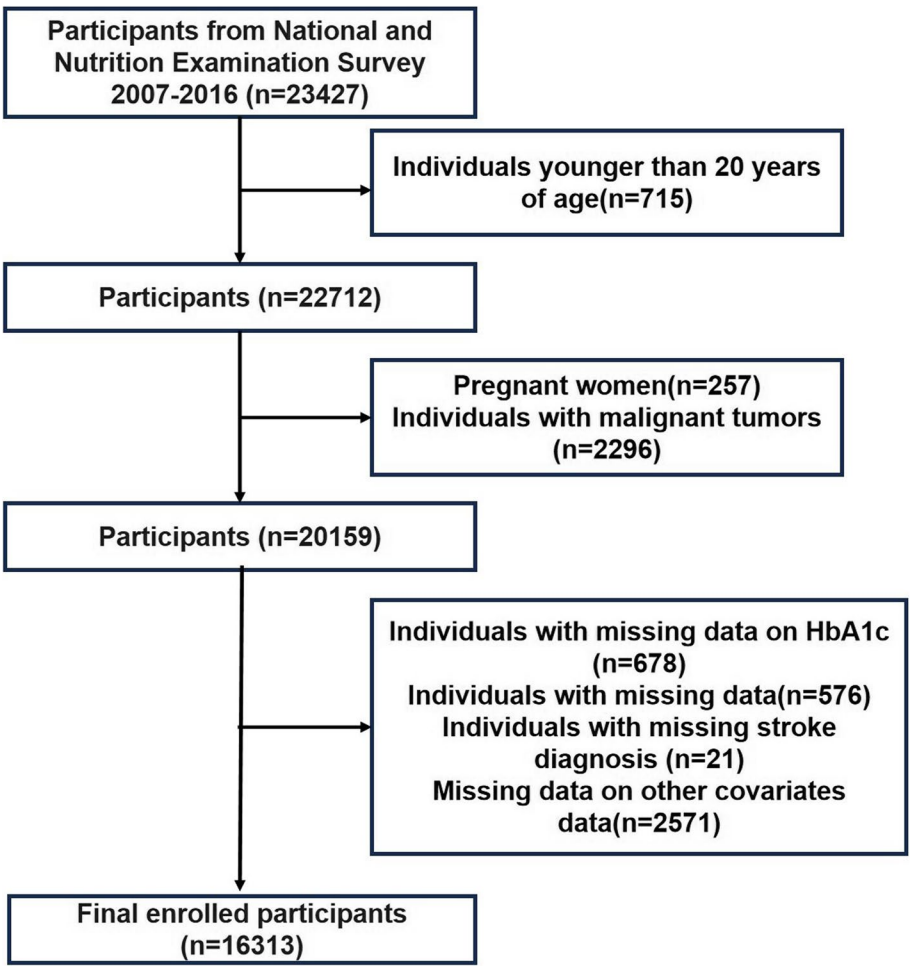

Fig. 1 Flowchart of the participant selection process

of hypertension, diabetes, cancer, or stroke ($n=202$); cancer patients ($n=98$); and individuals with a WC of 50 cm or less ($n=158$). Ultimately, 9,468 participants from CHARLS were eligible for cross-sectional analysis (Fig. 1).

Definition of eGDR

The eGDR was computed utilizing a recognized mathematical expression: $21.158-(0.551\times \mathrm{HbA1c})-(3.407\times \mathrm{HT})-(0.09\times \mathrm{WC})$. In this equation, HbA1c represents the percentage of glycosylated hemoglobin [27]. HT denotes hypertension status (coded as yes = 1 and no = 0) and is established through a physician's assessment. WC refers to the measurement of the waist, expressed in centimeters, taken at the natural waistline.

The study stratified all participants into four groups based on eGDR values, using the 25th, 50th, and 75th percentiles as cutoff points. The lowest quartile was chosen as the baseline group for comparison.

Definition of stroke

The study's primary endpoint was stroke occurrence, identified through patient-reported clinical diagnoses. Participants were questioned about any previous stroke confirmations from medical professionals. Those responding affirmatively were categorized as having a history of stroke [28].

Mortality assessment

To evaluate all-cause mortality, we utilized public mortality files linked to the National Death Index. The observation period was calculated from the date of examination at the Mobile Examination Center to the date of death or December 31, 2019, whichever occurred first. Causes of death were defined according to the codes of ICD-10 [29].

Covariables

Drawing on previous research [26, 30], covariables associated with stroke were included, including age

(< 50, ≥ 50), sex, race, schooling attainment (pre-college, partial college or associate credential, bachelor's or advanced degree), marital status (married, never married, other), poverty income ratio (PIR) (0–1.85, 1.86–3.50, > 3.50, representing low, middle, and high-income levels, respectively), alcohol consumption (yes, no), serum cotinine levels (0—limit of detection [LOD], LOD −10, > 10), body mass index (< 30, ≥ 30 kg/m2), the Healthy Eating Index (HEI) (inadequate, average, optimal), as well as diabetes (yes, no) and hypertension status (yes, no). Additionally, building upon prior literature, the HEI-2015 measures overall diet quality, scoring diets as "optimal" (> 80), "average" (51–80), or "inadequate" (< 50) based on a 10-component system [31, 32]. BMI was calculated as weight (kg) divided by the square of height (m). The information regarding diabetes and hypertension was derived from diagnoses reported by individuals based on their consultations with healthcare professionals [33].

Statistical analysis

Categorical variables were represented through counts and proportions and were compared by the χ^2 test between two different groups. eGDR was analyzed as a categorical variable and divided into quartile groups based on its 25th, 50th, and 75th percentiles. We conducted trend tests using the median value of each quartile of eGDR.The binary logistic regression model was applied to estimate the association between eGDR and stroke. The Cox proportional hazards model was used to calculate the hazard ratios (HR) and 95% confidence intervals (CI) for the association between eGDR and all-cause mortality.

We utilized three analytical frameworks: the baseline model, which operates without any modifications; Model 1, controlling for age and sex; and Model 2, which includes additional adjustments for race, education, PIR, marital status, serum cotinine levels, BMI, HEI, diabetes, hypertension, and alcohol consumption.

To elucidate the possible nonlinear association linking stroke association and eGDR, we utilized restricted cubic spline (RCS) curves. Subgroup analyses were conducted to assess the effects of eGDR on the incidence of stroke in several subgroups, including diabetes (yes/no) and hypertension(yes/no). Sensitivity analyses excluded participants with a stroke history within the past two years, with results validated against CHARLS data. Data processing and analyses were carried out utilizing R version 4.2.2 and SPSS version 27.0, supplemented by Zstats (version 1.0, www.zstats.net). We established statistical significance with a benchmark of $P < 0.05$.

Results

The baseline characteristics

Our study involved 16,313 participants, with 488 individuals having a history of stroke and 15,825 without. Table 1 summarizes the sociodemographic characteristics and clinical descriptive data for all participants across the two comparative groups. Analysis revealed significant disparities between the stroke and non-stroke cohorts across most baseline characteristics, except for gender, which showed no notable differences. Those who experienced a stroke skewed towards higher age brackets, predominantly non-Hispanic Black or White, less educated, from modest economic circumstances, smokers, and had poorer diet quality. Additionally, stroke subjects had more comorbidities, such as diabetes, obesity, and hypertension.

Association between eGDR and stroke

Our research indicates that as eGDR levels rise, the association of stroke appears to decrease (Table 2). We stratified eGDR into quartiles (Q1-Q4). Using Q1 as a reference, participants in Q4 exhibited a 60% lower odds of having a stroke in model 2 (OR = 0.40; 95% CI, 0.22–0.73, $P = 0.003$). Similarly, those in Q3 showed a decreased stroke association in comparison to Q1 (OR = 0.40; 95% CI, 0.23–0.69, $P = 0.001$). An examination of trends across all models revealed a noteworthy dose–response connection.

To further explore the nonlinear dynamics between eGDR and stroke association, RCS analyses were conducted, as depicted in Fig. 2. These analyses examined the relationship across the entire population and within subgroups categorized by gender. The RCS plots show similar nonlinear curves for both the total population and the female subgroup. In the total population, at an eGDR of 2.718, the least association of stroke was noted, while in females, the optimal eGDR was 2.720. Conversely, the male population exhibited a consistently negative trend without any distinct inflection point, indicating a different pattern of association. The turning points of the RCS curve for the entire population, male and female populations are located at eGDR = 8.52, 8.50, and 8.53, respectively, with 5 selected nodes.

Subgroup analysis

To illustrate whether the relationship between eGDR and stroke differs between individuals with and without diabetes, as well as those with and without hypertension, we conducted a subgroup analysis, as shown in Fig. 3. The study population was divided into groups based on diabetes status and hypertension status to analyze the association between eGDR and stroke. Among participants with hypertension, the effect of eGDR appeared weaker.

Table 1 NHANES 2007–2016: Comparative analysis of baseline features among participants based on stroke history

Characteristics	All participants (*n* = 16313)	No-Stroke (*n* = 15825)	Stroke *n* = 488	*P* value
Age (years)				< 0.001*
< 50	8752 (53.7)	8674 (54.8)	78 (16.0)	
≥ 50	7561 (46.3)	7151 (45.2)	410 (84.0)	
Sex				0.435
Male	8039 (49.3)	7807 (49.3)	232 (47.5)	
Female	8274 (50.7)	8018 (50.7)	256 (52.5)	
Race/ethnicity				< 0.001*
Non-Hispanic Black	3353 (20.6)	3223 (20.4)	130 (26.6)	
Non-Hispanic White	7128 (43.7)	6882 (43.5)	246 (50.4)	
Mexican American	2520 (15.4)	2465 (15.6)	55 (11.3)	
Other Hispanic	1689 (10.4)	1662 (10.5)	27 (5.5)	
Other Races[a]	1623 (9.9)	1593 (10.1)	30 (6.1)	
Education level				< 0.001*
Pre-college	7449 (45.7)	7140 (45.1)	309 (63.3)	
Partial college or associate credential	4853 (29.7)	4737 (29.9)	116 (23.8)	
Bachelor's or advanced degree	4011 (24.6)	3948 (24.9)	63 (12.9)	
Poverty-income ratio				< 0.001*
Low	7369 (45.2)	7090 (44.8)	279 (57.2)	
Middle	3878 (23.8)	3755 (23.7)	123 (25.2)	
High	5066 (31.1)	4980 (31.5)	86 (17.6)	
Marital Status				< 0.001*
Married	8503 (52.1)	8260 (52.2)	243 (49.8)	
Never married	3105 (19.0)	3064 (19.4)	41 (8.4)	
Other	4705 (28.8)	4501 (28.4)	204 (41.8)	
Drink				0.004*
No	4417 (27.1)	4257 (26.9)	160 (32.8)	
Yes	11896 (72.9)	11568 (73.1)	328 (67.2)	
Smoking (Serum cotinine category)(ng/ml)				0.008*
< LOD	4345 (26.6)	4219 (26.7)	126 (25.8)	
LOD-10	7939 (48.7)	7726 (48.8)	213 (43.6)	
> 10	4029 (24.7)	3880 (24.5)	149 (30.5)	
Body mass index (kg/m^2)				< 0.001*
< 30	9984 (61.2)	9727 (61.5)	257 (52.7)	
≥ 30	6329 (38.8)	6098 (38.5)	231 (47.3)	
Healthy eating index				0.028*
Inadequate	7855 (48.2)	7591 (48.0)	264 (54.1)	
Average	7293 (44.7)	7100 (44.9)	193 (39.5)	
Optimal	1165 (7.1)	1134 (7.2)	31 (6.4)	
Diabetes				< 0.001*
No	14367 (88.1)	14043 (88.7)	324 (66.4)	
Yes	1946 (11.9)	1782 (11.3)	164 (33.6)	
Hypertension				< 0.001*
No	10732 (65.8)	10616 (67.1)	116 (23.8)	
Yes	5581 (34.2)	5209 (32.9)	372 (76.2)	

Abbreviation: LOD Limit of detection

Data presented are mean ± SD or n (%)

* *P*<0.05. [a]Other races include Multi-Racial

Table 2 Associations between eGDR and stroke

	OR (95% CI), *P*		
Model	**Unadjusted**	**1**	**2**
Q1	-	-	-
Q2	0.54 (0.44, 0.66) <0.001*	0.64 (0.52, 0.78) <0.001*	0.90 (0.68, 1.19) 0.448
Q3	0.12 (0.08, 0.17) <0.001*	0.17 (0.12, 0.24) <0.001*	0.40 (0.23, 0.69) 0.001*
Q4	0.09 (0.06, 0.14) <0.001*	0.17 (0.12, 0.26) <0.001*	0.40 (0.22, 0.73) 0.003*
P for trend	<0.001*	<0.001*	0.004*

Q1: reference group; Model 1: sex and age were modified; Model 2: all covariables were modified

*$P<0.05$

eGDR demonstrated a stronger protective effect in the non-hypertensive group. For individuals with diabetes, the association was present but less pronounced, particularly in Model 3, indicating that the confounding factors included in the model influenced this association. In contrast, among non-diabetic participants, the association between eGDR and stroke was stronger.

Relationship between mortality and eGDR

The relationship between eGDR and mortality was assessed using Cox proportional hazards regression (Table 3). When eGDR was analyzed as categorical variables, the general population showed a decreased mortality in higher quartiles compared to Q1, as evidenced by the HRs of 0.74 (95% CI, 0.56–0.98; $P=0.035$) for Q3 and 0.71 (95% CI, 0.52–0.98; $P=0.037$) for Q4. For the non-stroke group, increased mortality was seen in Q2 and Q3 compared to Q1, with HRs of 1.40 (95% CI: 1.00–1.96; $P=0.048$) as well as 1.40 (95% CI, 1.08–1.81; $P=0.010$), respectively.

On the whole, Cox regression results pointed to eGDR as a negative predictor of overall mortality rates, applicable to both the general population and stroke-free groups, while this relationship was not significant among participants with stroke.

Sensitivity analysis

To address potential reverse causality effects, sensitivity analyses were performed by omitting individuals who manifested pertinent conditions during the initial two years of monitoring. The results, presented in Tables 4 and 5, indicate that the association between eGDR and stroke association remains generally consistent when eGDR is analyzed as a categorical variable. In Table 4, when eGDR was treated categorically, statistical significance was observed only in the third and fourth quartiles in Model 2. Specifically, in Model 2, OR for stroke association in the third eGDR quartile was 0.34 (95% CI: 0.18–0.62, $P=0.001$) and 0.37 (95% CI: 0.19–0.73, $P=0.004$) in the fourth quartile, indicating a significant protective association at higher eGDR quartiles.

Similarly, sensitivity analysis using the CHARLS 2011 dataset (Table 5) showed a negative association between eGDR and stroke in the unadjusted and Model 1. However, in Model 2, the association between each eGDR quartile and stroke lost statistical significance. This suggests that the protective effect of eGDR on stroke association may be sensitive to specific adjustment methods and population characteristics.

Discussion

Our study highlights several key findings regarding the impact of eGDR on stroke association and all-cause mortality. Firstly, utilizing a multivariate logistic model, we identified eGDR as a protective factor against stroke. This relationship persisted even after comprehensive adjustment for confounders.

Secondly, the Cox hazards model unveiled a negative relationship linking all-cause mortality and eGDR levels in both the overall population and the group without pre-existing conditions. Notably, eGDR emerged as a particularly sharp indicator of mortality association among participants without a history of stroke. For these individuals, metabolic factors may directly influence mortality association, as they are not confounded by stroke-related complications and comorbidities. In contrast, in patients with stroke history, the stroke itself constitutes a high-risk mortality event, with post-stroke complications potentially becoming the primary determinants of survival, thus diminishing the impact of eGDR. Additionally, stroke patients may receive more medical interventions, including pharmacotherapy and rehabilitation, which could significantly affect mortality and potentially obscure the influence of eGDR.

Thirdly, RCS analysis indicated the presence of a nonlinear relationship between eGDR levels and the likelihood of experiencing a stroke, with different curve patterns observed in men and women, suggesting a

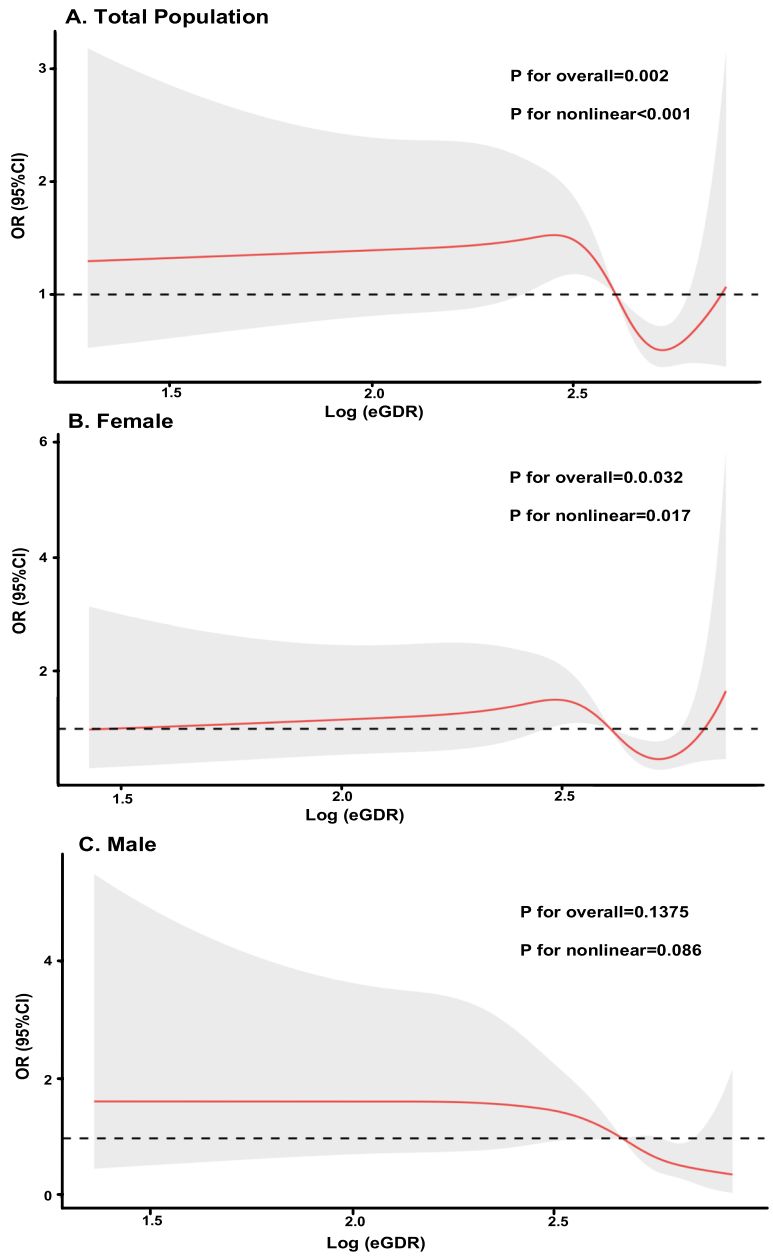

Fig. 2 Restricted cubic spline curve for the relationship between eGDR and stroke relationship. **A** Entire Cohort; (**B**) Female Participants; (**C**) Male Participants. Red lines represent odds ratios and gray areas denote 95% confidence intervals

potential influence of sex hormones [34]. A population-based study from Denmark indicated that while metabolic syndrome and diabetes are known to raise the ischemic stroke association in both genders, these risk factors appear to have a greater impact on women [35]. A clinical study from Spain suggests that elderly women exhibit unique risk factors and distribution patterns of subtypes in acute ischemic stroke, including a higher proportion of cardioembolic strokes and poorer prognosis, accompanied by higher mortality rates, severe cognitive impairment, and multiple hospital complications [36]. Moreover, female-specific physiological factors such as oral contraceptive use [37], pregnancy [38], and pregnancy-related complications [39], further contribute to sex differences in stroke association.

Fourthly, higher eGDR levels correspond to a lower likelihood of stroke occurrence. The findings from both Chinese and American populations consistently support

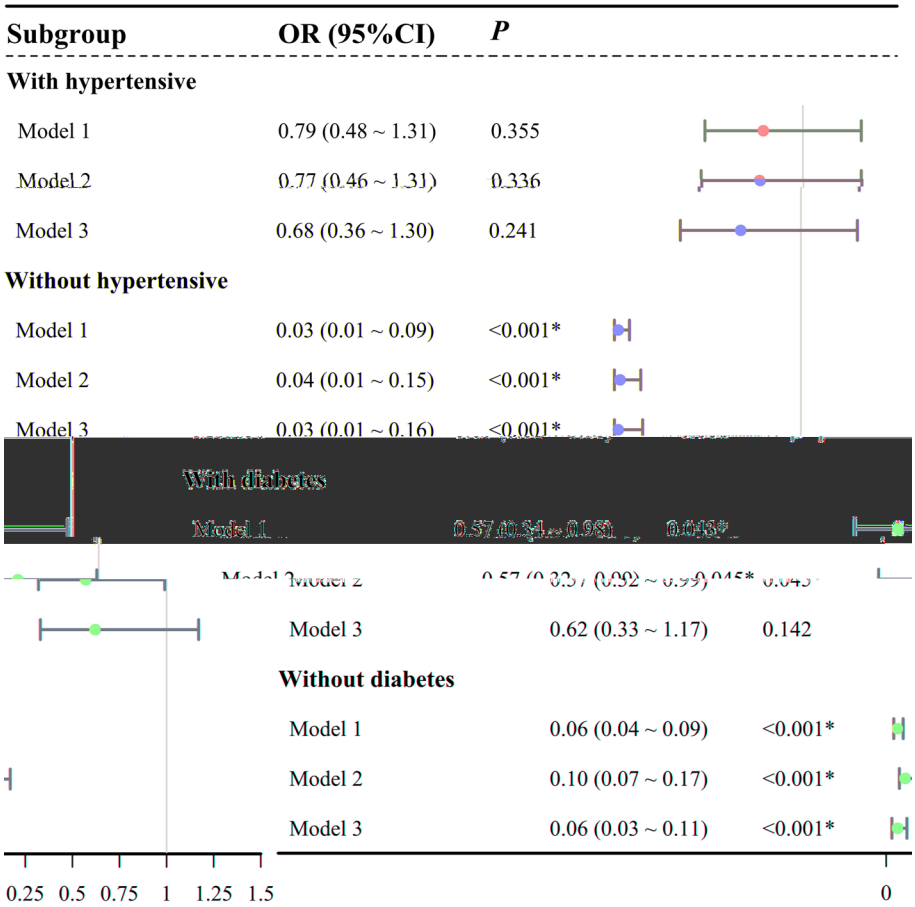

Fig. 3 Subgroup analysis of multi-variable adjusted association of eGDR with stroke. Model 1: Non-modified model; Model 2: sex and age were modified; Model 3: all covariables were modified.*$P < 0.05$

Table 3 Cox regression analysis of eGDR's association with mortality

	HR (95% CI), *P*		
	Total	**Without stroke**	**With stroke**
Q1	-	-	-
Q2	1.04 (0.88, 1.22), 0.667	1.40 (1.00, 1.96), 0.048*	1.26 (0.79, 2.01), 0.334
Q3	0.74 (0.56, 0.98), 0.035*	1.40 (1.08, 1.81), 0.010*	0.79 (0.28, 2.23), 0.652
Q4	0.71 (0.52, 0.98), 0.037*	1.03 (0.82, 1.30), 0.783	0.60 (0.17, 2.11), 0.428
P for trend	0.89 (0.80, 0.99), 0.033*	0.89 (0.80, 1.00), 0.040*	0.95 (0.67, 1.35), 0.765

Q1: reference; *$P < 0.05$

this association. However, after multivariate adjustments, this association lost its significance when analyzed as continuous variables, indicating that other variables may have influenced it.

Recent investigations have shed light on the relationship between eGDR and stroke association. One notable study, drawing data from the CHARLS, examined this association in a population of mature and elderly participants. This research examined a standardized sample of 4,790 participants, utilizing K-means cluster analysis to classify eGDR levels. The results demonstrated that higher eGDR levels correlated positively with stroke occurrence, with a discernible linear trend, which suggests that poorly controlled eGDR levels significantly increase stroke association [40]. A longitudinal study with 1,476 participants found that elevated eGDR values

Table 4 Sensitivity analysis of the eGDR-stroke association in NHANES 2007–2016

	OR (95% CI), *P*		
Model	**Unadjusted**	**1**	**2**
Q1	-	-	-
Q2	0.51 (0.40, 0.64), < 0.001*	0.60 (0.47, 0.75), < 0.001*	0.81 (0.59, 1.10), 0.174
Q3	0.11 (0.07, 0.16), < 0.001*	0.16 (0.10, 0.24), < 0.001*	0.34 (0.18, 0.62), 0.001*
Q4	0.10 (0.06, 0.15), < 0.001*	0.18 (0.11, 0.28), < 0.001*	0.37 (0.19, 0.73), 0.004*
P for trend	0.42 (0.37, 0.47), < 0.001*	0.50 (0.44, 0.57), < 0.001*	0.71 (0.57, 0.89), 0.003*

Q1: reference; Model 1: sex and age were modified; Model 2: all covariables were modified

* $P < 0.05$

Table 5 Sensitivity analysis of the eGDR-stroke association in CHARLS 2011

	OR (95% CI), *P*		
Model	**Unadjusted**	**1**	**2**
Q1	-	-	-
Q2	0.28 (0.19, 0.40), < 0.001*	0.30 (0.21, 0.44), < 0.001*	0.89 (0.47, 1.71), 0.734
Q3	0.19 (0.12, 0.29), < 0.001*	0.21 (0.13, 0.32), < 0.001*	0.75 (0.33, 1.68),0.481
Q4	0.21 (0.14, 0.32), < 0.001*	0.22 (0.15, 0.34), < 0.001*	0.81 (0.36, 1.81),0.609
P for trend	0.53 (0.46, 0.61), < 0.001*	0.54 (0.47, 0.62), < 0.001*	0.94 (0.74, 1.20),0.618

Q1: reference; Model 1: sex and age were modified; Model 2: all covariables were modified

* $P < 0.05$

corresponded with a lower likelihood of stroke occurrence, cardiac events, and cardiovascular disease [25]. Besides, a cohort study conducted in Sweden involving 104,697 Type 2 diabetes patients identified eGDR as an inverse predictor of stroke likelihood, with HRs of 0.77 (0.69–0.87), 0.68 (0.58–0.80), and 0.60 (0.48–0.76) for eGDR levels of 4–6, 6–8, and above 8, respectively, and this link was unaffected by clinical characteristics and other known dangerous factors [21]. A Chinese retrospective cohort study provided additional evidence indicating that a higher eGDR was correlated with better 3-month and 1-year outcomes in stroke patients regarding stroke recurrence, functional recovery, and vascular events [41]. These studies align with our findings.

Our research has several strengths. Firstly, it employs extensive and representative data from across the United States, thereby augmenting the applicability of our results to the wider U.S. population. Secondly, we accounted for confounding variables and conducted sensitivity analyses to ensure result robustness. We also explored nonlinear effects in female participants, highlighting gender differences often overlooked in clinical practice. Lastly, our findings were validated using data from a Chinese database, where consistent results across two cohort studies further reinforced our conclusions.

Despite these strengths, several limitations warrant consideration. The study's cross-sectional nature presents inherent limitations in establishing causality and raises the potential for reverse causation. Thus, prospective studies with a considerable number of subjects are imperative. Although we adjusted for several potential covariables, the influence of unmeasured confounding variables cannot be entirely excluded. Moreover, our analysis is based on U.S. and Chinese databases, and differences in racial diversity and age distribution between the CHARLS and NHANES study populations may account for variations in results. The applicability of these findings to other races or countries requires further investigation. Due to the lack of detailed imaging data, this study could not analyze outcomes by vascular territory. Stroke prognosis varies by region, with posterior cerebral artery infarctions generally having a better prognosis than middle cerebral artery infarctions [42]. Future studies should include imaging data to explore the relationship between eGDR and specific stroke subtypes. In this study, information regarding the diagnosis of stroke, diabetes, and hypertension was based on self-reported diagnoses after consultations with medical professionals, which may introduce potential bias. We plan to use more objective diagnostic methods in future research.

Therefore, there is an urgent need to validate these findings in a larger and more diverse population. Future research should strive to determine optimal eGDR threshold values for eGDR for clinical practice and develop management strategies for both stroke and non-stroke patients regarding eGDR.

Conclusion

The eGDR demonstrated a negative association with stroke association and mortality. Our findings suggest that eGDR is a protective factor against stroke and a valid predictor of stroke.

Abbreviations

BMI	Body Mass Index
CHARLS	China Health and Retirement Longitudinal Study
eGDR	Estimated Glucose Disposal Rate
HbA1c	Glycosylated Hemoglobin
HDL	High Density Lipoprotein
HEI	The Healthy Eating Index
IR	Insulin Resistance
LOD	Limit of Detection
NHANES	National Health and Nutrition Examination Survey
PIR	Poverty Income Ratio
RCS	Restricted Cubic Spline Curves
T1D	Type 1 Diabetes
WC	Waist Circumference

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Authors' contributions

YT, KX, LY, BW, YW, and QC were responsible for the study's conception and design. YT, HY, and KX analyzed the data. The initial manuscript was drafted by YT and KX, with subsequent revisions by YL and CG. All authors have reviewed and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The NHANES study received ethical approval from the Research Ethics Review Board of the NCHS. All NHANES participants or their legal guardians provided written informed consent. The CHARLS study was approved by the Institutional Review Board of Peking University (approval numbers: IRB00001052-11015 for household survey and IRB00001052-11014 for blood sample collection). Written consent was obtained from all CHARLS participants.

Competing interests

The authors declare no competing interests.

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