Cardiovascular Diabetology

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Stress hyperglycemia ratio and the risk of new-onset chronic diseases: results of a national prospective longitudinal study

Zhuang Ma[1†], Lanlan Wu[1†] and Zheng Huang[1*]

Abstract

Background The stress hyperglycemia ratio (SHR), a dynamic biomarker of acute glucose dysregulation, has been established as a predictor of adverse acute outcomes. However, its longitudinal associations with chronic disease development, particularly in middle-aged and older populations, remain insufficiently characterized.

Methods This nationwide prospective cohort study analyzed data from 8942 adults aged ≥ 45 years in the China Health and Retirement Longitudinal Study (CHARLS). We established 14 disease-specific cohorts to the relationship between SHR and new-onset chronic conditions. Multivariable-adjusted Cox proportional hazards models with restricted cubic splines were utilized to estimate hazard ratios (HRs) per standard deviation (SD) increase in SHR, supported by comprehensive sensitivity analyses and subgroup stratifications.

Results Elevated SHR levels were significantly associated with increased risks of incident hypertension (HR = 1.30, 95% CI: 1.06–1.60; $P < 0.001$), dyslipidemia (HR = 1.43, 95% CI: 1.17–1.74; $P < 0.001$), diabetes (HR = 2.30, 95% CI: 1.82–2.91; $P < 0.001$), and liver disease (HR = 1.65, 95% CI: 1.21–2.26; $P = 0.002$). Conversely, elevated SHR levels correlated with a lower risk of lung disease (HR = 0.67, 95% CI: 0.50–0.89; $P = 0.006$). Restricted cubic spline analyses revealed a nonlinear relationship between SHR and diabetes risk (P-nonlinear = 0.02), while linear associations were observed for other outcomes. Subgroup analyses demonstrated consistency across demographic strata (P-interaction > 0.05).

Conclusions SHR demonstrates disease-specific associations with chronic disease development, indicating its potential value as a predictive marker for clinical risk assessment.

Keywords SHR, Chronic disease, Longitudinal study, CHARLS

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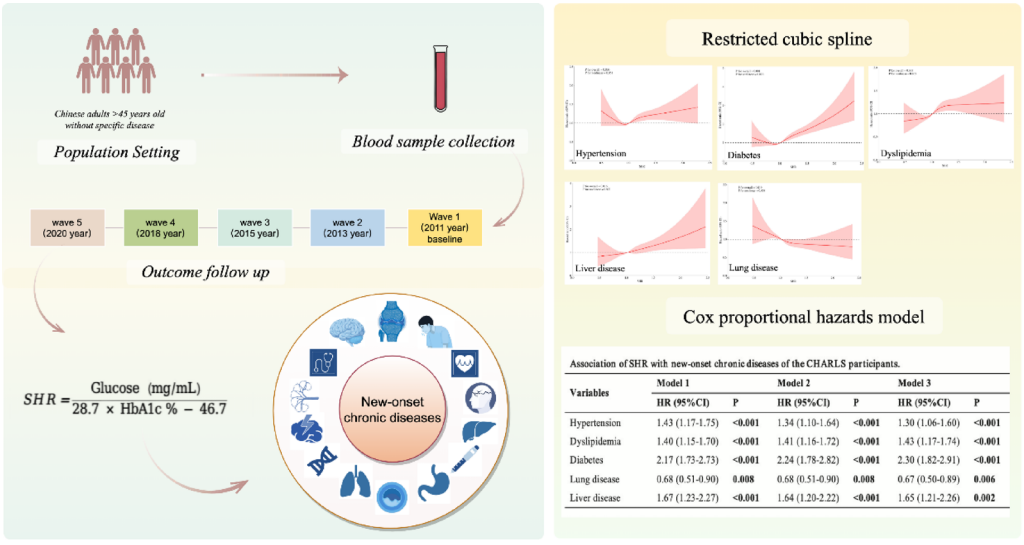
Graphical abstract



Association of SHR with new-onset chronic diseases of the CHARLS participants.

Variables	Model 1		Model 2		Model 3	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Hypertension	1.43 (1.17-1.75)	<0.001	1.34 (1.10-1.64)	<0.001	1.30 (1.06-1.60)	<0.001
Dyslipidemia	1.40 (1.15-1.70)	<0.001	1.41 (1.16-1.72)	<0.001	1.43 (1.17-1.74)	<0.001
Diabetes	2.17 (1.73-2.73)	<0.001	2.24 (1.78-2.82)	<0.001	2.30 (1.82-2.91)	<0.001
Lung disease	0.68 (0.51-0.90)	0.008	0.68 (0.51-0.90)	0.008	0.67 (0.50-0.89)	0.006
Liver disease	1.67 (1.23-2.27)	<0.001	1.64 (1.20-2.22)	<0.001	1.65 (1.21-2.26)	0.002

Conclusion: Elevated stress hyperglycemia ratio (SHR) was significantly associated with increased risks of new-onset hypertension, diabetes, dyslipidemia, and liver disease, but paradoxically linked to a reduced risk of lung disease.

Research insights

What is currently known about this topic?

1. The SHR, a biomarker indicating acute glucose dysregulation, has been established as a predictor of adverse acute outcomes, such as mortality in acute myocardial infarction and sepsis. However, its longitudinal associations with chronic disease development, particularly in middle-aged and older populations, remain inadequately characterized.
2. Previous studies focused primarily on short-term outcomes, with limited evidence regarding SHR's role in long-term chronic disease risk.

What is the key research question?

Does elevated SHR independently predict heterogeneous risks of incident chronic diseases (e.g., hypertension, diabetes, dyslipidemia) in middle-aged and older adults, and are these associations disease-specific?

What is new?

1. Elevated SHR demonstrated significant associations with increased risks of new-onset hypertension, diabetes, dyslipidemia, and liver disease but unexpectedly correlated with a reduced risk of lung disease.
2. A nonlinear relationship was observed between SHR and diabetes risk, whereas linear associations were found for other outcomes.
3. This study extends SHR's application beyond acute settings, establishing it as a novel biomarker for risk stratification of chronic disease in aging populations.

How might this study influence clinical practice?

1. SHR is a cost-effective tool for identifying individuals at high risk of chronic diseases and facilitating early interventions, such as lifestyle modifications and glucose monitoring.
2. Clinicians may incorporate SHR into routine risk assessments to develop targeted preventive strategies for conditions like diabetes and hypertension.

Introduction

Chronic diseases represent the primary contributor to global mortality and disability, placing unsustainable burdens on healthcare systems worldwide [1]. Recent epidemiological transitions indicate that non-communicable diseases account for 74% of global deaths, with aging populations showing disproportionate vulnerability [2]. Among modifiable risk factors, stress-induced hyperglycemia—a transient elevation in blood glucose during acute physiological stress—has emerged as a crucial yet understudied mediator of chronic disease pathogenesis [3], particularly in middle-aged and older adults. Observed clinically in critical illness, major surgery, and trauma [4], this phenomenon correlates with adverse outcomes, including increased mortality [5, 6], infection susceptibility [7], and extended hospitalization [8].

The stress hyperglycemia ratio (SHR), calculated as admission glucose normalized by HbA1c, serves as a dynamic biomarker indicating acute glycemic dysregulation [9]. Mechanistic studies indicate that SHR influences disease progression through multiple pathways, including endothelial dysfunction, systemic inflammation enhancement, and insulin resistance intensification [10, 11]. Clinical evidence demonstrates SHR's prognostic significance across various acute conditions [12–14]. A meta-analysis encompassing 26 cohort studies ($n = 87{,}974$) revealed that elevated SHR during acute myocardial infarction substantially increased the risk of major adverse cardiovascular and cerebrovascular events, long-term all-cause mortality, and in-hospital mortality [15]. In sepsis patients, SHR showed a U-shaped relationship with 28-day mortality (AUC = 0.83; P-nonlinear < 0.01), indicating dual functions in immune modulation and metabolic stress [16].

While the evidence linking SHR to acute outcomes continues to accumulate, its longitudinal associations with chronic disease development remain inadequately explored—a significant gap considering the "metabolic memory" phenomenon [17]. Initial findings suggest enduring effects: a retrospective study of patients with acute myocardial infarction found that elevated SHR levels correlated significantly with increased risk of new-onset atrial fibrillation (OR: 1.05, 95% CI: 1.01–1.10) [18]. Additionally, elevated SHR has emerged as an independent predictor of incident type 2 diabetes (T2D) [19]. However, comprehensive population-based studies systematically examining SHR's predictive capacity across diverse chronic diseases remain limited.

This study seeks to address these knowledge gaps through a prospective analysis of middle-aged and older adults from the China Health and Retirement Longitudinal Study (CHARLS). We hypothesize that elevated SHR independently predicts varying risks of incident chronic diseases. Our research aims to establish SHR as a novel biomarker for chronic disease risk stratification and guide targeted prevention strategies.

Methods

Study population and design

This study constitutes a secondary analysis of longitudinal cohort data. The data were derived from five waves of the CHARLS conducted between 2011 and 2020 [20]. CHARLS focuses on Chinese residents aged ≥ 45 years, aiming to investigate population aging and track health, economic, and social changes in middle-aged and older adults. The study employs a four-stage stratified cluster sampling method. Specifically, the sampling is based on Probability Proportional to Size (PPS), where the probability of selection is proportional to the population size. Participants were recruited from 450 communities across 150 county-level units in 28 provinces of China. Biennial surveys are conducted using standardized equipment to measure physical parameters and blood biomarkers. The present analysis utilized publicly available data from the CHARLS study, which received prior ethical approval from the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015). As this research represents a secondary analysis of de-identified data, additional ethics approval was not necessary. The study adheres to the original study's ethical guidelines.

For this analysis, participants were excluded if they had incomplete SHR data ($n = 6{,}718$), missing chronic disease information ($n = 530$), or incomplete covariate data ($n = 2{,}058$). Each chronic disease cohort comprised participants free of the respective disease at baseline with complete follow-up data. A flowchart illustrating participant selection appears in Fig. 1.

Chronic disease assessment

For each chronic disease cohort, incident cases were identified when participants responded affirmatively to the question, "Has a doctor ever diagnosed you with [specific disease]?" during follow-up assessments [21]. The onset time was defined as the midpoint between the follow-up wave at which the diagnosis occurred and the participant's most recent prior follow-up [22]. Incident diabetes cases were identified through self-reported physician diagnoses. The diabetes diagnosis relied on self-reporting without distinguishing between type 1 and type 2 diabetes.

SHR definition

The calculation formula of SHR was [23]:

$$SHR = \frac{\text{Glucose (mg/mL)}}{28.7 \times \text{HbA1c \%} - 46.7}$$

In the CHARLS study, blood samples were collected from participants after an overnight fast (≥ 8 h) using standardized protocols. Plasma glucose levels were measured enzymatically (hexokinase method), and HbA1c was quantified via high-performance liquid chromatography (HPLC) using a Tosoh G8 analyzer.

Based on the respective SHR values, the participants were stratified into four quartiles: Q1: 0.18 ≤ SHR < 0.93, Q2: 0.93 ≤ SHR < 1.02, Q3: 1.02 ≤ SHR < 1.14, Q4: 1.14 ≤ SHR < 6.34.

Covariates

Baseline covariates were collected through standardized questionnaires and physical examinations. During the initial assessment wave (2011), information was gathered regarding age, gender, marital status, education level, hukou status, alcohol status, and smoking status. Marital

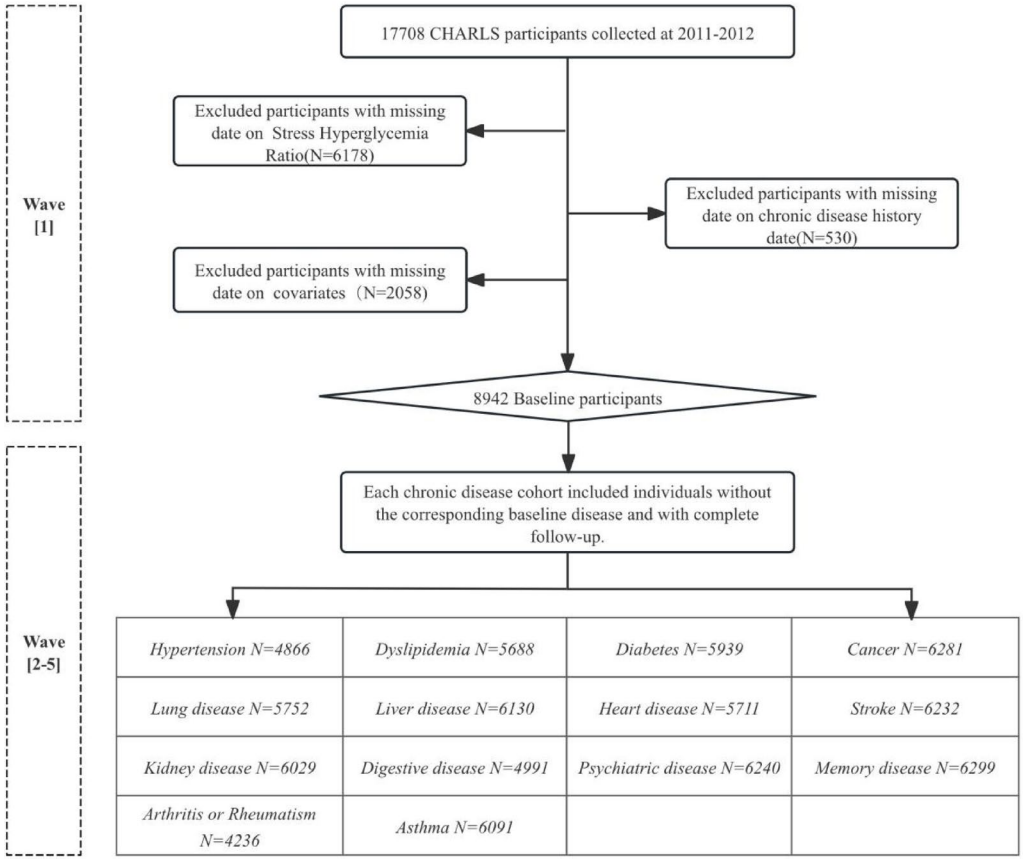


Fig. 1 Flow diagram of the screening of the CHARLS participants

status was classified as married or other, education as below or above middle school, and hukou status as rural or urban. Smoking and alcohol use were categorized as never, former, or current. self-rated health was measured through a standardized question, "How would you rate your health?", and responses were categorized as Poor, General, or good based on predefined survey options. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Laboratory measurements included low-density lipoprotein cholesterol (LDL), creatinine (CR), and C-reactive protein (CRP). To address the potential confounding effects of pre-existing conditions on outcomes, the history of 14 chronic diseases was incorporated as covariates in each disease cohort, excluding the specific disease under investigation. This adjustment aimed to control for the effects of baseline disease history on subsequent health outcomes [21].

The covariate selection reflects established pathological mechanisms of high blood pressure and hyperglycemia, insulin resistance and inflammation, as well as the sociodemographic characteristics of the CHARLS cohort, ensuring comprehensive control for individual biological, behavioral, and environmental confounding factors.

Statistical analyses

Baseline characteristics were stratified by SHR quartiles. Continuous variables are presented as means ± standard deviations (SD) and analyzed using ANOVA (for normally distributed data) or the Kruskal-Wallis H test (for non-normal data). Laboratory measurements included fasting glucose, HbA1c, LDL, CR, and CRP, with values expressed as mean ± standard deviation (SD). Categorical variables are presented as counts and percentages, with between-group differences evaluated using Pearson's chi-square test (unordered categories) or Cochran-Armitage trend test (ordered categories). Cox proportional hazards models assessed the association between SHR and new-onset chronic disease risk. Model 1 remained unadjusted, including no covariates. Model 2 adjusted for age, gender, and hukou status, while Model 3 additionally adjusted for marital status, education, alcohol consumption, smoking status, BMI, CR, LDL, CRP, and the history of 14 baseline chronic conditions (excluding the specific chronic disease under investigation in each cohort) [21]. Restricted cubic splines (RCS) models with four nodes (three internal nodes) at the 5th, 35th, 65th, and 95th percentiles of the SHR variable were applied to account for potential non-linear associations. Kaplan-Meier survival curves estimated survival probabilities across SHR quartiles, with

log-rank tests comparing survival differences between groups. Subgroup analyses examined variations by gender, age (≤65 years or >65 years), hukou status, marital status, education level, alcohol consumption, and smoking status. A sensitivity analysis excluding participants who experienced the outcome event during the first follow-up (Wave 2) addressed potential reverse causality bias. All statistical analyses utilized R version 4.3.3 and Zstats 1.0 (www.zstats.net). Statistical significance was defined as a two-tailed p-value < 0.05.

Results

Population characteristics

Table 1 presents the baseline characteristics of participants stratified by SHR quartiles. The study included 8,942 participants, with a mean age of 59.55 (SD 9.34) years, comprising 46.60% males and 53.40% females. The mean baseline SHR was 1.06 (SD 0.24). Higher SHR quartiles demonstrated significant differences in several baseline characteristics ($P < 0.05$). Participants in the higher SHR group were predominantly male, urban residents, more educated, and showed higher rates of current alcohol consumption and former smoking. Physiologically, the higher SHR group exhibited significantly elevated BMI, CRP, and serum creatinine levels compared to lower quartiles. This group also demonstrated a higher prevalence of hypertension, diabetes, and dyslipidemia while showing a lower prevalence of lung disease, gastrointestinal disorders, arthritis, and asthma. Comparative baseline characteristics between completers and participants lost to follow-up across new-onset chronic diseases cohorts are comprehensively documented in Supplementary Table 16.

Association between the SHR and new-onset chronic diseases

As demonstrated in Table 2, elevated SHR levels exhibited significant associations with increased risks of new-onset hypertension (HR = 1.43, 95% CI = 1.17–1.75, $P < 0.001$), diabetes (HR = 2.17, 95% CI = 1.73–2.73, $P < 0.001$), dyslipidemia (HR = 1.40, 95% CI = 1.15–1.70, $P < 0.001$), and liver disease (HR = 1.67, 95% CI = 1.23–2.27, $P = 0.003$). Conversely, higher SHR levels correlated with decreased risks of new-onset lung disease (HR = 0.68, 95% CI = 0.51–0.90, $P = 0.008$) and new-onset arthritis (HR = 0.78, 95% CI = 0.62–0.98, $P = 0.032$). These associations maintained statistical significance in the fully adjusted model for all outcomes except new-onset arthritis. Analysis stratified by SHR quartiles indicated that participants in the highest quartile, compared to those in the lowest quartile, demonstrated significantly higher risks of new-onset hypertension (HR = 1.15, 95% CI = 1.01–1.31, $P = 0.034$), dyslipidemia (HR = 1.25, 95% CI = 1.09–1.43, $P < 0.001$), diabetes (HR = 1.50, 95% CI = 1.26–1.79, $P = 0.001$), and liver disease (HR = 1.29, 95% CI = 1.03–1.61, $P = 0.025$). Notably, participants in the highest SHR quartile showed a significantly lower risk of new-onset lung disease compared to the lowest quartile (HR = 0.81, 95% CI = 0.69–0.96, $P = 0.013$). These trends demonstrated statistical significance (all $P < 0.05$), as detailed in Table S1.

Furthermore, RCS analysis (Fig. 2) revealed a significant nonlinear relationship between SHR and new-onset diabetes risk (P for nonlinearity = 0.02), while linear associations were identified for hypertension, dyslipidemia, liver disease, and lung disease (P for nonlinearity > 0.05). Figure 3 presents the Kaplan-Meier survival curves for new-onset chronic diseases stratified by SHR quartiles, showing significant differences in the incidence of new-onset hypertension, diabetes, dyslipidemia, and lung disease during follow-up (log-rank $P < 0.001$).

Subgroup analyses

The research included subgroup analyses to evaluate potential effect modification by gender, age, marital status, education level, hukou status, smoking, alcohol consumption, and baseline health status. The relationship between SHR and new-onset chronic disease risk remained consistent across subgroups, with no significant interaction effects observed (Table S3–S16; all P-values for interaction > 0.05), except for interactions between smoking status and cancer incidence, and between gender and digestive diseases. Sensitivity analyses excluding participants who experienced the outcome event during the first follow-up (Wave 2) confirmed the robustness of these findings (Table 3).

Discussion

This nationwide longitudinal study illuminates the dual role of SHR in chronic disease pathogenesis among middle-aged and older Chinese adults. The findings demonstrate that an one-standard-deviation increase in SHR increases the risks of hypertension (HR = 1.30), diabetes mellitus (HR = 2.30), dyslipidemia (HR = 1.43), and hepatic disorders (HR = 1.65) while simultaneously reducing the incidence of pulmonary diseases (HR = 0.67). These associations maintained consistency across multivariable adjustments for covariates and comprehensive sensitivity and subgroup analyses.

Stress-induced hyperglycemia represents a complex physiological response characterized by acute blood glucose fluctuations, accompanied by neurohormonal alterations and fluid imbalances [24]. Although typically considered transient and adaptive, emerging evidence indicates that SHR correlates with adverse long-term health outcomes. Mamtani et al. demonstrated that in critically ill patients, SHR exhibits a U-shaped relationship with both short-term and long-term mortality, with

Table 1 Baseline characteristics of the CHARLS participants by SHR index quartile

Variables	Total (*n* = 8942)	Q1 (*n* = 2233)	Q2 (*n* = 2238)	Q3 (*n* = 2232)	Q4 (*n* = 2239)	*P*
Age, years	59.55 (9.34)	59.62 (9.28)	59.37 (9.39)	59.27 (9.35)	59.94 (9.32)	0.081
Sex, no. (%)						**0.037**
Female	4775 (53.40)	1198 (53.65)	1224 (54.69)	1215 (54.44)	1138 (50.83)	
Male	4167 (46.60)	1035 (46.35)	1014 (45.31)	1017 (45.56)	1101 (49.17)	
Hukou status, no (%)						**< 0.001**
Urban	1568 (17.54)	331 (14.82)	391 (17.47)	424 (19.00)	422 (18.85)	
Rural	7374 (82.46)	1902 (85.18)	1847 (82.53)	1808 (81.00)	1817 (81.15)	
Education, no (%)						**0.047**
Less than high school	6280 (70.23)	1615 (72.32)	1578 (70.51)	1535 (68.77)	1552 (69.32)	
High school and above	2662 (29.77)	618 (27.68)	660 (29.49)	697 (31.23)	687 (30.68)	
Marry, no (%)						**0.868**
Others	1113 (12.45)	285 (12.76)	272 (12.15)	284 (12.72)	272 (12.15)	
Married	7829 (87.55)	1948 (87.24)	1966 (87.85)	1948 (87.28)	1967 (87.85)	
Self-comment of your health, No (%)						**0.968**
Low	2498 (27.94)	629 (28.17)	622 (27.79)	622 (27.87)	625 (27.91)	
Moderate	4522 (50.57)	1128 (50.52)	1146 (51.21)	1132 (50.72)	1116 (49.84)	
Good	1922 (21.49)	476 (21.32)	470 (21.00)	478 (21.42)	498 (22.24)	
Drinking status, no (%)						**0.002**
Never	5262 (58.85)	1341 (60.05)	1327 (59.29)	1319 (59.09)	1275 (56.95)	
Former	762 (8.52)	195 (8.73)	217 (9.70)	188 (8.42)	162 (7.24)	
Now	2918 (32.63)	697 (31.21)	694 (31.01)	725 (32.48)	802 (35.82)	
Smoking status, no (%)						**0.019**
Never	5428 (60.70)	1329 (59.52)	1377 (61.53)	1386 (62.10)	1336 (59.67)	
Former	799 (8.94)	175 (7.84)	194 (8.67)	217 (9.72)	213 (9.51)	
Now	2715 (30.36)	729 (32.65)	667 (29.80)	629 (28.18)	690 (30.82)	
BMI (kg/m^2)	23.51 (3.92)	23.30 (4.01)	23.38 (3.64)	23.65 (4.02)	23.70 (3.97)	**< 0.001**
CRP (mg/L)	2.79 (7.79)	2.73 (7.57)	2.67 (7.30)	2.53 (6.08)	3.23 (9.75)	**0.017**
Serum creatinine (mg/dl)	0.78 (0.24)	0.78 (0.21)	0.77 (0.19)	0.78 (0.18)	0.81 (0.34)	**< 0.001**
LDL (mg/dL)	116.65 (34.94)	117.63 (31.81)	119.40 (33.96)	117.04 (34.90)	112.53 (38.43)	**< 0.001**
Hypertension, no (%)	2382 (26.64)	538 (24.09)	553 (24.71)	619 (27.73)	672 (30.01)	**< 0.001**
Dyslipidemia, no (%)	883 (9.87)	166 (7.43)	200 (8.94)	257 (11.51)	260 (11.61)	**< 0.001**
Diabetes, no (%)	553 (6.18)	104 (4.66)	100 (4.47)	127 (5.69)	222 (9.92)	**< 0.001**
Cancer, no (%)	72 (0.81)	15 (0.67)	16 (0.71)	22 (0.99)	19 (0.85)	0.639
Lung disease, no (%)	883 (9.87)	249 (11.15)	230 (10.28)	205 (9.18)	199 (8.89)	**0.043**
Liver disease, no (%)	302 (3.38)	82 (3.67)	81 (3.62)	70 (3.14)	69 (3.08)	0.574
Heart disease, no (%)	1079(12.07)	289(12.94)	246(10.99)	263(11.78)	281(12.55)	0.194
Stroke, no (%)	224 (2.51)	50 (2.24)	56 (2.50)	58 (2.60)	60 (2.68)	0.800
Kidney disease, no (%)	525 (5.87)	139 (6.22)	126 (5.63)	139 (6.23)	121 (5.40)	0.544
Digestive disease, no (%)	2018 (22.57)	549 (24.59)	505 (22.56)	492 (22.04)	472 (21.08)	**0.039**
Psychiatric disease, no (%)	113 (1.26)	27 (1.21)	30 (1.34)	33 (1.48)	23 (1.03)	0.575
Memory disease, no (%)	133 (1.49)	33 (1.48)	32 (1.43)	39 (1.75)	29 (1.30)	0.649
Arthritis or rheumatism, n(%)	3108 (34.76)	840 (37.62)	764 (34.14)	749 (33.56)	755 (33.72)	**0.012**
Asthma, no (%)	420 (4.70)	129 (5.78)	109 (4.87)	89 (3.99)	93 (4.15)	**0.019**

BMI body mass index, *LDL* low density lipoprotein, *CRP* C-reactive protein

Continuous variables are presented as mean ± standard deviation (SD), values in bold indicate p <0.05

a critical threshold at SHR = 0.96 [25, 26]. Sustained glucose fluctuations under prolonged stress conditions may intensify metabolic dysfunction, particularly in individuals with pre-existing chronic diseases [27]. Research in diabetic and prediabetic populations has identified a U-shaped or L-shaped association between SHR and mortality [28], Furthermore, chronic stress from environmental exposures—including air pollution, socioeconomic strain, and occupational hazards—may contribute to sustained metabolic dysregulation in community-dwelling populations. Studies have demonstrated that SHR follows a U-shaped pattern in relation to all-cause mortality among community residents [29, 30], This study advances prior research by evaluating

Table 2 Association of SHR with new-onset chronic diseases of the CHARLS participants

Variables	Model 1		Model 2		Model 3	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
Hypertension	1.43 (1.17–1.75)	**< 0.001**	1.34 (1.10–1.64)	**< 0.001**	1.30 (1.06–1.60)	**< 0.001**
Dyslipidemia	1.40 (1.15–1.70)	**< 0.001**	1.41 (1.16–1.72)	**< 0.001**	1.43 (1.17–1.74)	**< 0.001**
Diabetes	2.17 (1.73–2.73)	**< 0.001**	2.24 (1.78–2.82)	**< 0.001**	2.30 (1.82–2.91)	**< 0.001**
Cancer	1.35 (0.80–2.25)	0.26	1.32 (0.79–2.23)	0.289	1.25 (0.74–2.12)	0.395
Lung disease	0.68 (0.51–0.90)	**0.008**	0.68 (0.51–0.90)	**0.008**	0.67 (0.50–0.89)	**0.006**
Liver disease	1.67 (1.23–2.27)	**< 0.001**	1.64 (1.20–2.22)	**< 0.001**	1.65 (1.21–2.26)	**0.002**
Heart disease	0.92 (0.71–1.18)	0.491	0.87 (0.68–1.13)	0.299	0.88 (0.68–1.13)	0.311
Stroke	1.22 (0.90–1.67)	0.199	1.18 (0.87–1.61)	0.291	1.14 (0.84–1.55)	0.396
Kidney disease	1.04 (0.76–1.40)	0.821	0.97 (0.72–1.32)	0.861	0.99 (0.73–1.35)	0.970
Digestive disease	0.93 (0.74–1.18)	0.552	0.95 (0.75–1.20)	0.688	1.08 (0.86–1.35)	0.517
Psychiatric disease	0.70 (0.40–1.23)	0.217	0.71 (0.41–1.25)	0.241	0.84 (0.48–1.47)	0.54
Memory disease	0.95 (0.65–1.39)	0.799	0.91 (0.62–1.33)	0.615	0.93 (0.63–1.36)	0.703
Arthritis or rheumatism	0.78 (0.62–0.98)	**0.032**	0.79 (0.62–0.99)	**0.041**	0.84 (0.67–1.06)	0.138
Asthma	1.07 (0.71–1.63)	0.736	1.13 (0.76–1.68)	0.533	1.08 (0.72–1.62)	0.695

CI confidence interval, *HR* hazard ratio, values in bold indicate p <0.05

Model 1: Crude model

Model 2: Adjusted for age, sex, Hukou Status

Model 3: Adjusted for age, sex, marry, education, Hukou Status, drinking, smoking, BMI, CR, LDL, CRP, and the history of 14 chronic diseases at baseline (excluding the specific chronic disease under investigation in each cohort)

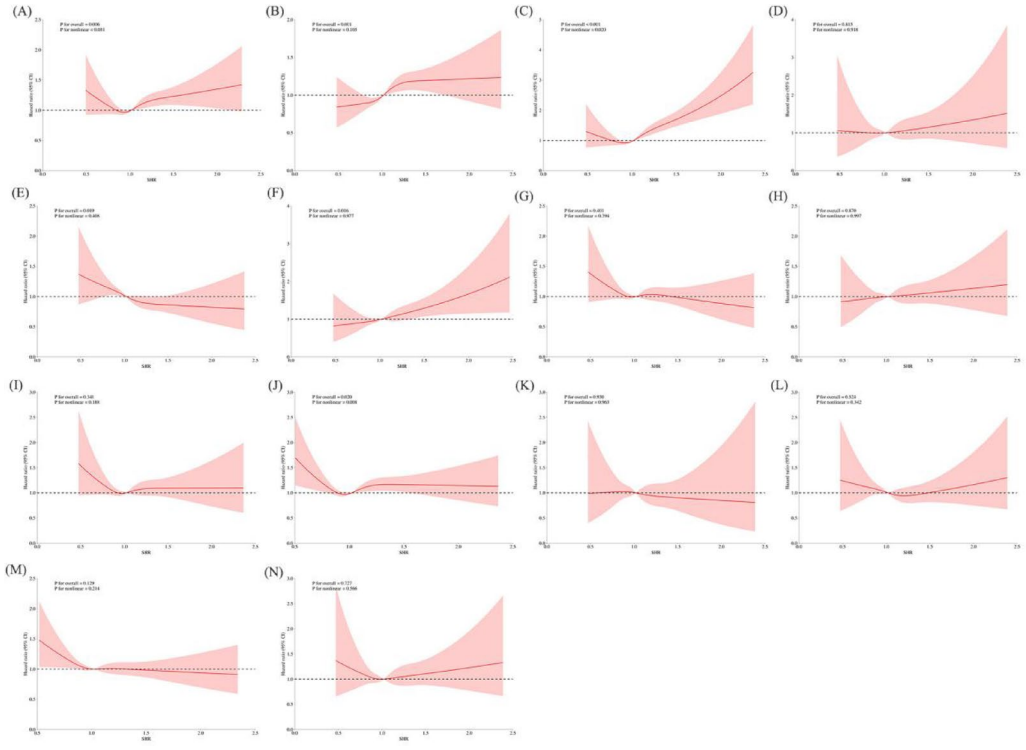


Fig. 2 Association of SHR index with new-onset chronic diseases of the CHARLS participants by RCS. The model adjusted for age, sex, marry, education, working, drinking, smoking, BMI, systolic blood pressure, diastolic blood pressure, LDL, CRP, and the history of 14 chronic diseases at baseline (excluding the specific chronic disease under investigation in each cohort). CHARLS, China Health and Retirement Longitudinal Study, CMI, cardiometabolic index. **A** Hypertension; **B** Dyslipidemia; **C** Diabetes; **D** Cancer; **E** Lung disease; **F** Liver disease; **G** Heart disease; **H** Stroke; **I** Kidney disease; **J** Digestive disease; **K** Psychiatric disease; **L** Memory disease; **M** Arthritis or Rheumatism; **N** Asthma

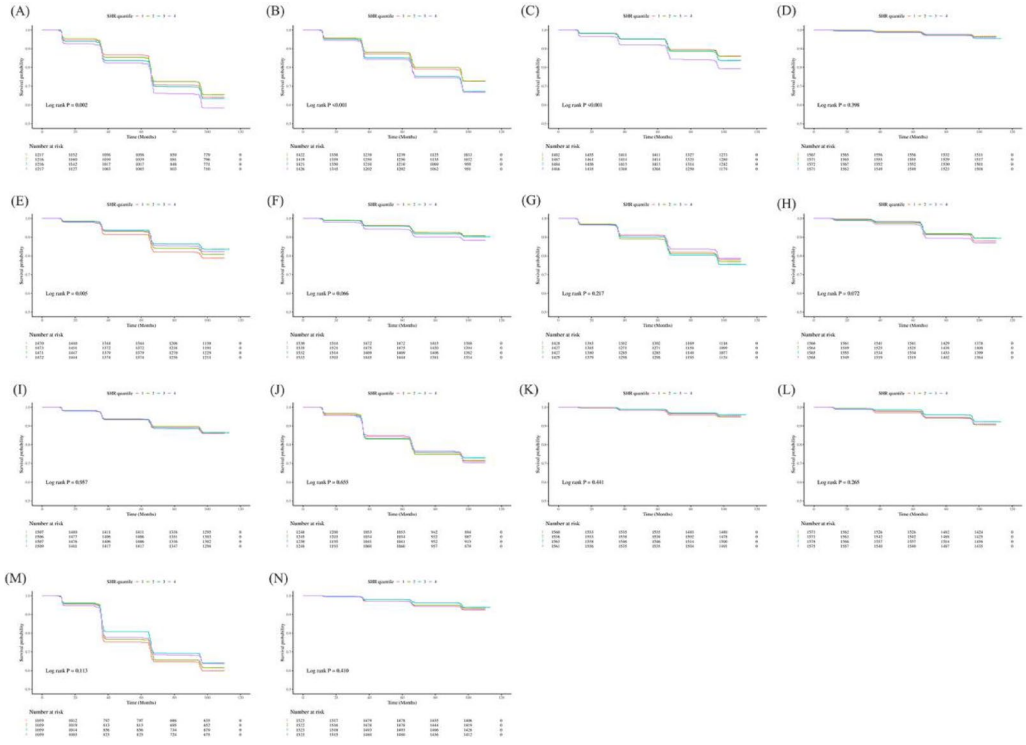


Fig. 3 Kaplan-Meier survival curve for new-onset chronic diseases of CHARLS participants by SHR index quartile. CHARLS, China Health and Retirement Longitudinal Study, CMI, cardiometabolic index. **A** Hypertension; **B** Dyslipidemia; **C** Diabetes; **D** Cancer; **E** lung disease; **F** Liver disease; **G** Heart disease; **H** Stroke; **I** Kidney disease; **J** Digestive disease; **K** Psychiatric disease; **L** Memory disease; **M** Arthritis or Rheumatism; **N** Asthma

Table 3 Association of SHR with new-onset chronic diseases of the CHARLS participants after excluding participants who experienced outcome events during wave 2

Variables	Model 1		Model 2		Model 3	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
Hypertension	1.33 (1.06–1.66)	**0.014**	1.25 (1.00-1.56)	0.053	1.21 (0.96–1.52)	0.1
Dyslipidemia	1.37 (1.10–1.70)	**0.005**	1.34 (1.07–1.67)	**0.002**	1.42 (1.14–1.76)	**0.004**
Diabetes	1.87 (1.44–2.44)	**< 0.001**	1.91 (1.47–2.50)	**< 0.001**	1.98 (1.50–2.59)	**< 0.001**
Cancer	1.29 (0.74–2.23)	0.368	1.27 (0.73–2.20)	0.405	1.22 (0.70–2.13)	0.480
Lung disease,	0.67 (0.49–0.91)	**0.008**	0.68 (0.51–0.91)	**0.008**	0.67 (0.49–0.90)	**0.006**
Liver disease	1.47 (1.04–2.07)	**0.029**	1.43 (1.01–2.02)	**0.043**	1.43 (1.01–2.04)	**0.043**
Heart disease	0.88 (0.67–1.16)	0.375	0.83 (0.63–1.10)	0.193	0.85 (0.64–1.12)	0.238
Stroke	1.14 (0.82–1.58)	0.428	1.09 (0.79–1.50)	0.612	1.08 (0.78–1.49)	0.650
Kidney disease	1.05 (0.75–1.45)	0.788	1.03 (0.75–1.43)	0.837	0.99 (0.72–1.38)	0.972
Digestive disease	0.95 (0.74–1.22)	0.694	1.10 (0.86–1.40)	0.444	1.11 (0.87–1.41)	0.398
Psychiatric disease	0.66 (0.37–1.18)	0.164	0.76 (0.43–1.36)	0.361	0.79 (0.44–1.42)	0.425
Memory disease	0.85 (0.57–1.28)	0.447	0.83 (0.55–1.25)	0.379	0.84 (0.56–1.27)	0.415
Arthritis or rheumatism	0.72 (0.56–0.93)	**0.011**	0.79 (0.62–1.02)	0.066	0.77 (0.60–0.99)	**0.043**
Asthma	1.06 (0.68–1.63)	0.808	1.12 (0.74–1.69)	0.583	1.07 (0.70–1.63)	0.748

CI confidence interval, *HR* hazard ratio, values in bold indicate p <0.05

Model 1: Crude model

Model 2: Adjusted for age, sex, Hukou Status

Model 3: Adjusted for age, sex, marry, education, Hukou Status, drinking, smoking, BMI, CR, LDL, CRP, and the history of 14 chronic diseases at baseline (excluding the specific chronic disease under investigation in each cohort)

the relationship between SHR and incident chronic disease risk, expanding beyond acute outcomes. The results establish SHR as a potential biomarker for chronic disease pathogenesis, highlighting its clinical relevance in long-term health risk assessment and disease prevention strategies. The observed disease associations align with three interrelated pathophysiological axes mediated by stress hyperglycemia:

Insulin resistance cascade

Research demonstrates that chronic stress activates both the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, resulting in endocrine changes, including increased cortisol and catecholamine secretion. These hormonal changes influence glucose and lipid metabolism [31, 32] and insulin sensitivity [33–36]. The consequences of these intricate interactions not only promote hyperglycemia and IR [37–39] but also elevate the risk of metabolic disorders, including diabetes and dyslipidemia [40, 41].

Oxidative-inflammatory axis

Monnier [42] demonstrates that hyperglycemia induces oxidative stress, as evidenced by elevated urinary excretion of 8-iso PGF2α in diabetic patients. Animal studies have revealed that acute glucose infusion suppresses immune function while promoting cytokine secretion and hepatic oxidative stress responses [43, 44]. SHR intensifies inflammation by activating pro-inflammatory mediators, including TNF-α, IL-6, and CRP, thus contributing to chronic low-grade inflammation. This inflammatory condition exacerbates tissue damage and increases hepatic glucose release, creating a self-perpetuating cycle of metabolic dysregulation [45–48]. Furthermore, hyperglycemia disrupts vascular homeostasis by disturbing the balance between vasodilators (NO, PGI2) and vasoconstrictors (endothelin and angiotensin II). These alterations lead to upregulation of core binding factor α subunit 1 and bone morphogenetic protein-2, promoting vascular smooth muscle cell calcification [49], Such processes contribute to abnormal vascular tension and endothelial dysfunction [50], establishing a mechanistic link between stress hyperglycemia and vascular injury [51–53].

Epigenetic mechanisms and the "metabolic memory" phenomenon

SHR also induces epigenetic modifications, including DNA methylation and histone modifications, driven by the accumulation of reactive oxygen species (ROS) and advanced glycation end products (AGEs). These epigenetic changes affect metabolic states immediately and, through sustained gene regulation, establish a "metabolic memory" that maintains metabolic dysregulation, even after glycemic normalization [17]. This remodeling provides a mechanistic explanation for the persistent disease risk associated with stress hyperglycemia, highlighting its role in the development and progression of chronic metabolic diseases despite subsequent improvements in blood glucose levels.

The study findings support these proposed mechanisms, where elevated SHR levels correlate with hypertension, diabetes, dyslipidemia, and chronic liver disease. These associations can be mechanistically explained through stress-induced disruption of glucose and lipid metabolism, abnormal vascular tension, and oxidative stress triggered by hyperglycemia.

Pulmonary protection hypothesis

The inverse association between SHR and lung diseases in our study presents a paradox, particularly considering the established links between elevated SHR and pneumonia mortality. Previous research indicates that high SHR represents a significant risk factor for mortality in elderly patients with community-acquired pneumonia [54] and correlates independently with more severe COVID-19 outcomes, with patients in the high SHR group showing worse symptoms compared to those with low SHR ($p = 0.004$) [55], This paradox may be attributed to several factors. While high SHR typically indicates metabolic dysregulation, it may also represent a compensatory adaptive response, enhancing lung defense mechanisms under certain conditions. Stress-induced hyperglycemia can stimulate the release of stress hormones and pro-inflammatory mediators, which may, in some cases, strengthen immune responses and improve lung resistance to infections or injury. Additionally, geospatial confounding from environmental factors, such as particulate matter (PM2.5), air pollution, and occupational hazards, could influence both SHR and lung disease outcomes, potentially distorting the observed relationship. These environmental exposures affect both metabolic health and respiratory function, potentially contributing to residual confounding. Future studies should consider environmental covariates and pulmonary biomarkers to better clarify this complex relationship.

Cardiovascular paradox

Our study did not identify a significant association between SHR and cardiovascular diseases or stroke. This inconsistency may be attributed to multiple factors. Previous research has established SHR as a reliable predictor of adverse cardiovascular outcomes in both diabetic and non-diabetic populations [56–60], demonstrating a J-shaped or U-shaped relationship with short-term and long-term mortality [12, 61, 62]. Furthermore, SHR has been independently linked to brain edema, poor functional outcomes, and increased acute post-ischemic stroke mortality following cerebral infarction [63–65]. However, these investigations primarily examined mortality rates, which may explain the divergence in our findings, as our study focused on disease incidence rather than mortality rates. Additionally, research on chronic β-adrenergic activation indicates that while catecholamine infusion partially activates apoptotic pathways in cardiomyocytes, complete activation of the apoptosis cascade requires additional stress signals or factors [66].

This suggests that the absence of a significant SHR-cardiovascular disease correlation in our study may result from compensatory mechanisms that mitigate cardiac damage, with full apoptotic activation requiring additional stressors. Thus, while SHR reflects metabolic dysregulation, its impact on cardiovascular disease may be more complex and dependent on other contributory factors not captured in our analysis.

The innovation of this study lies in its utilization of large-scale, nationally representative longitudinal data to examine the association between SHR and the risk of 14 chronic diseases. Our findings indicate that SHR functions not only as a physiological marker of stress response but also as a novel, cost-effective biomarker for predicting multiple chronic diseases. However, this study presents several limitations. First, the diagnosis of chronic diseases and covariates relied on self-reported data, potentially introducing recall bias. Some participants may have undiagnosed or subclinical conditions, affecting the accuracy of our findings. Future research should incorporate objective diagnostic measures, including biomarkers and clinical assessments, to enhance reliability. Second, as the study population was drawn primarily from China, the findings may not be fully generalizable to other populations with different demographic and epidemiological profiles. Further validation in diverse populations is warranted. Thirdly, the diagnosis of diabetes relied on self-report without differentiation between type 1 and type 2 diabetes. However, given the cohort's age range and the high prevalence of T2D in middle-aged and older Chinese adults, our findings likely reflect associations with T2D. Fourthly, our study excluded participants with missing data or loss to follow-up. While sensitivity analyses suggested robustness, excluded individuals were older and had slightly worse baseline health profiles. This may slightly underestimate the true associations, particularly for conditions like diabetes and hypertension. Future studies with enhanced retention strategies are needed to generalize findings to the most vulnerable populations. Additionally, data structure limitations precluded assessment of longitudinal SHR trajectories and their disease outcome associations, as well as potential interactions among the 14 comorbidities. Although multiple confounders were controlled for, residual confounding cannot be ruled out. Subgroup analysis indicated that most interactions were not significant, the heterogeneity of smoking and cancer, gender, and digestive diseases suggested that future studies should explore the synergistic effects of SHR with behavioral/biological factors. Future studies should employ longitudinal trajectory analyses and causal inference methods to further elucidate SHR's role in chronic disease progression.

Conclusion

In this nationwide prospective longitudinal study, SHR demonstrates distinct longitudinal associations with chronic disease pathogenesis, particularly exhibiting strong diabetogenic effects. The paradoxical inverse association with pulmonary disorders warrants further investigation. These findings position SHR as a potential polyvalent biomarker for risk stratification of chronic diseases in aging populations.

Supplementary Information

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Supplementary Material 1

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Author contributions

ZH and LL W designed the study. LL W organized the data, conducted the analyses, and wrote and edited the manuscript. ZH and ZM critically revised the manuscipt for important intellectual content. All authors have reviewed and approved the final version of the manuscript.

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Data availability

Publicly available datasets were analyzed in this study. This data can be found here: The China Health and Retirement Longitudinal Study can be publicly accessed at https://charls.pku.edu.cn/.

Declarations

Competing interests

The authors declare no competing interests.

Ethics statement

All participants in the China Health and Retirement Longitudinal Study (CHARLS) provided informed consent, and the study protocol was approved by the Ethical Review Committee of Peking University (IRB00001052-11015). The study was conducted in accordance with local regulations and institutional guidelines. Written informed consent for participation was not required from the participants or their legal guardians/next of kin, in compliance with national legislation and institutional requirements.

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References

1. Ferrari AJ et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the global burden of disease study 2021. Lancet. 2024;403(10440):2133–61.

2. World Health O. World health statistics 2023: monitoring health for the sdgs, sustainable development goals. Geneva: World Health Organization; 2023.
3. Dungan KM, Braithwaite SS, Preiser JC. Stress Hyperglycaemia Lancet. 2009;373(9677):1798–807.
4. Capes SE, et al. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet. 2000;355(9206):773–8.
5. Kosiborod M, et al. Admission glucose and mortality in elderly patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation. 2005;111(23):3078–86.
6. Umpierrez GE, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. J Clin Endocrinol Metab. 2002;87(3):978–82.
7. Stegenga ME, et al. Hyperglycemia enhances coagulation and reduces neutrophil degranulation, whereas hyperinsulinemia inhibits fibrinolysis during human endotoxemia. Blood. 2008;112(1):82–9.
8. van den Berghe G, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001;345(19):1359–67.
9. Roberts GW, et al. Relative hyperglycemia, a marker of critical illness: introducing the stress hyperglycemia ratio. J Clin Endocrinol Metab. 2015;100(12):4490–7.
10. Ceriello A, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes. 2008;57(5):1349–54.
11. Ceriello A, et al. Effect of postprandial hypertriglyceridemia and hyperglycemia on Circulating adhesion molecules and oxidative stress generation and the possible role of Simvastatin treatment. Diabetes. 2004;53(3):701–10.
12. Xu W, et al. Association of stress hyperglycemia ratio and in-hospital mortality in patients with coronary artery disease: insights from a large cohort study. Cardiovasc Diabetol. 2022;21(1):217.
13. Sia CH, et al. Optimal glucose, HbA1c, glucose-HbA1c ratio and stress-hyperglycaemia ratio cut-off values for predicting 1-year mortality in diabetic and non-diabetic acute myocardial infarction patients. Cardiovasc Diabetol. 2021;20(1):211.
14. Kerby JD, et al. Stress-induced hyperglycemia, not diabetic hyperglycemia, is associated with higher mortality in trauma. Ann Surg. 2012;256(3):446–52.
15. Karakasis P, et al. Prognostic value of stress hyperglycemia ratio in patients with acute myocardial infarction: a systematic review with bayesian and frequentist meta-analysis. Trends Cardiovasc Med. 2024;34(7):453–65.
16. Yan F, et al. Association between the stress hyperglycemia ratio and 28-day all-cause mortality in critically ill patients with sepsis: a retrospective cohort study and predictive model establishment based on machine learning. Cardiovasc Diabetol. 2024;23(1):163.
17. Cooper ME, El-Osta A. Epigenetics: mechanisms and implications for diabetic complications. Circ Res. 2010;107(12):1403–13.
18. Luo J, et al. Association of stress hyperglycemia ratio with in-hospital new-onset atrial fibrillation and long-term outcomes in patients with acute myocardial infarction. Diabetes Metab Res Rev. 2024;40(2):e3726.
19. Cui C, et al. The additive effect of the stress hyperglycemia ratio on type 2 diabetes: a population-based cohort study. Cardiovasc Diabetol. 2025;24(1):5.
20. Zhao Y, et al. Cohort profile: the China health and retirement longitudinal study (CHARLS). Int J Epidemiol. 2014;43(1):61–8.
21. Zhuo L, et al. Cardiometabolic index and the risk of new-onset chronic diseases: results of a National prospective longitudinal study. Front Endocrinol (Lausanne). 2024;15:1446276.
22. Li H, et al. Association of depressive symptoms with incident cardiovascular diseases in Middle-Aged and older Chinese adults. JAMA Netw Open. 2019;2(12):e1916591.
23. Nathan DM, et al. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008;31(8):1473–8.
24. Aronson D, et al. Usefulness of changes in fasting glucose during hospitalization to predict long-term mortality in patients with acute myocardial infarction. Am J Cardiol. 2009;104(8):1013–7.
25. Li L, et al. Prognostic significance of the stress hyperglycemia ratio in critically ill patients. Cardiovasc Diabetol. 2023;22(1):275.
26. Badawi O, et al. Association between intensive care unit-acquired dysglycemia and in-hospital mortality. Crit Care Med. 2012;40(12):3180–8.
27. Ferreira JA, et al. Admission hyperglycemia and all-cause mortality in diabetic and non-diabetic patients with acute myocardial infarction: a tertiary center analysis. Intern Emerg Med. 2021;16(8):2109–19.
28. Ding L, et al. The prognostic value of the stress hyperglycemia ratio for all-cause and cardiovascular mortality in patients with diabetes or prediabetes: insights from NHANES 2005–2018. Cardiovasc Diabetol. 2024;23(1):84.
29. Qiu S, et al. Association between the stress-hyperglycemia ratio and all-cause mortality in community-dwelling populations: an analysis of the National health and nutrition examination survey (NHANES) 1999–2014. J Diabetes. 2024;16(6):e13567.
30. Li J, Yu C, Hu X. What is the optimal range of fasting stress hyperglycemia ratio for all-cause mortality in American adults: an observational study. Med (Baltim). 2024;103(43):e40288.
31. Klein J, et al. beta(3)-adrenergic stimulation differentially inhibits insulin signaling and decreases insulin-induced glucose uptake in brown adipocytes. J Biol Chem. 1999;274(49):34795–802.
32. Kelley DE, et al. Interaction between glucose and free fatty acid metabolism in human skeletal muscle. J Clin Invest. 1993;92(1):91–8.
33. Black PH. The inflammatory response is an integral part of the stress response: implications for atherosclerosis, insulin resistance, type II diabetes and metabolic syndrome X. Brain Behav Immun. 2003;17(5):350–64.
34. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev. 2000;21(1):55–89.
35. McEwen BS. Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. Eur J Pharmacol. 2008;583(2–3):174–85.
36. Chrousos GP. Stress and disorders of the stress system. Nat Rev Endocrinol. 2009;5(7):374–81.
37. Paolisso P, et al. Impact of admission hyperglycemia on heart failure events and mortality in patients with Takotsubo syndrome at Long-term Follow-up: data from HIGH-GLUCOTAKO investigators. Diabetes Care. 2021;44(9):2158–61.
38. Shamoon H, Hendler R, Sherwin RS. Synergistic interactions among antiinsulin hormones in the pathogenesis of stress hyperglycemia in humans. J Clin Endocrinol Metab. 1981;52(6):1235–41.
39. Dünser MW, Hasibeder WR. Sympathetic overstimulation during critical illness: adverse effects of adrenergic stress. J Intensive Care Med. 2009;24(5):293–316.
40. Barth E, et al. Glucose metabolism and catecholamines. Crit Care Med. 2007;35(9 Suppl):S508–18.
41. Andrews RC, Walker BR. Glucocorticoids and insulin resistance: old hormones, new targets. Clin Sci (Lond). 1999;96(5):513–23.
42. Monnier L, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA. 2006;295(14):1681–7.
43. Kwoun MO, et al. Immunologic effects of acute hyperglycemia in nondiabetic rats. JPEN J Parenter Enter Nutr. 1997;21(2):91–5.
44. Ling PR, et al. Hyperglycemia induced by glucose infusion causes hepatic oxidative stress and systemic inflammation, but not STAT3 or MAP kinase activation in liver in rats. Metabolism. 2003;52(7):868–74.
45. Cheng S, et al. Association between stress hyperglycemia ratio index and all-cause mortality in critically ill patients with atrial fibrillation: a retrospective study using the MIMIC-IV database. Cardiovasc Diabetol. 2024;23(1):363.
46. Morohoshi M, et al. Glucose-dependent Interleukin 6 and tumor necrosis factor production by human peripheral blood monocytes in vitro. Diabetes. 1996;45(7):954–9.
47. Heesen M, et al. Can the interleukin-6 response to endotoxin be predicted? Studies of the influence of a promoter polymorphism of the interleukin-6 gene, gender, the density of the endotoxin receptor CD14, and inflammatory cytokines. Crit Care Med. 2002;30(3):664–9.
48. Ritchie DG. Interleukin 6 stimulates hepatic glucose release from prelabeled glycogen pools. Am J Physiol. 1990;258(1 Pt 1):E57–64.
49. Chen NX, et al. High glucose increases the expression of Cbfa1 and BMP-2 and enhances the calcification of vascular smooth muscle cells. Nephrol Dial Transpl. 2006;21(12):3435–42.
50. Nishikawa T, et al. Normalizing mitochondrial superoxide production blocks three pathways of hyperglycaemic damage. Nature. 2000;404(6779):787–90.
51. Yan H, et al. Associations between cardiometabolic indices and the risk of diabetic kidney disease in patients with type 2 diabetes. Cardiovasc Diabetol. 2024;23(1):142.
52. Lai W, et al. Association of stress hyperglycemia ratio with presence and severity of chronic kidney disease among US adults with diabetes mellitus. Front Endocrinol (Lausanne). 2024;15:1446390.

53. Ferroni P, et al. Platelet activation in type 2 diabetes mellitus. J Thromb Haemost. 2004;2(8):1282–91.
54. Miao L, et al. Stress hyperglycemia ratio and its influence on mortality in elderly patients with severe community-acquired pneumonia: a retrospective study. Aging Clin Exp Res. 2024;36(1):175.
55. Cheng Y, et al. Stress hyperglycemia is associated with disease severity in COVID-19. Endokrynol Pol. 2023;74(5):528–35.
56. Yang J, et al. The impact of the stress hyperglycemia ratio on Short-term and Long-term poor prognosis in patients with acute coronary syndrome: insight from a large cohort study in Asia. Diabetes Care. 2022;45(4):947–56.
57. Zhang C, et al. Relationship between stress hyperglycemia ratio and allcause mortality in critically ill patients: results from the MIMIC-IV database. Front Endocrinol (Lausanne). 2023;14:1111026.
58. Liu J, et al. Impact of stress hyperglycemia ratio on mortality in patients with critical acute myocardial infarction: insight from American MIMIC-IV and the Chinese CIN-II study. Cardiovasc Diabetol. 2023;22(1):281.
59. Song Y, et al. High triglyceride-glucose index and stress hyperglycemia ratio as predictors of adverse cardiac events in patients with coronary chronic total occlusion: a large-scale prospective cohort study. Cardiovasc Diabetol. 2023;22(1):180.
60. Cui K, et al. The impact of fasting stress hyperglycemia ratio, fasting plasma glucose and hemoglobin A1c on in-hospital mortality in patients with and without diabetes: findings from the China acute myocardial infarction registry. Cardiovasc Diabetol. 2023;22(1):165.
61. Wei QC, et al. Association of stress hyperglycemia with clinical outcomes in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention: a cohort study. Cardiovasc Diabetol. 2023;22(1):85.
62. Chen G, et al. Association between stress hyperglycemia ratio and In-hospital outcomes in elderly patients with acute myocardial infarction. Front Cardiovasc Med. 2021;8:698725.
63. Pan H, et al. Association between stress hyperglycemia ratio with short-term and long-term mortality in critically ill patients with ischemic stroke. Acta Diabetol. 2024;61(7):859–68.
64. Deng Y, et al. The stress hyperglycemia ratio is associated with the development of cerebral edema and poor functional outcome in patients with acute cerebral infarction. Front Aging Neurosci. 2022;14:936862.
65. Jiang Z, et al. Association between stress hyperglycemia ratio and prognosis in acute ischemic stroke: a systematic review and meta-analysis. BMC Neurol. 2024;24(1):13.
66. Dostanic S, et al. Chronic beta-adrenoreceptor stimulation in vivo decreased Bcl-2 and increased Bax expression but did not activate apoptotic pathways in mouse heart. Can J Physiol Pharmacol. 2004;82(3):167–74.

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