European Review for Medical and Pharmacological Sciences 2022; 26: 9258-9269

Association of the stress hyperglycemia ratio and clinical outcomes in patients with cardiovascular diseases: a systematic review and meta-analysis

Y.-W. HUANG[1], Y.-H. AN[2], X.-S. YIN[3], Z.-P. LI[1]

[1]Department of Neurosurgery, [2]Center of Reproductive Medicine, [3]Department of Immunology, School of Medicine, University of Electronic Science and Technology of China, Mianyang Central Hospital, Mianyang, Sichuan, China

Abstract. – OBJECTIVE: Cardiovascular disease (CVD) and cerebrovascular disease are the leading cause of death around the world all the time. A novel marker described as the stress hyperglycemia ratio (SHR) can reflect the acute hyperglycemic status and is associated with poor outcomes in patients with acute illness, such as stroke and myocardial infarction (MI). Our previous study has shown that SHR was strongly related to the clinical outcomes of stroke patients. Nevertheless, the association between SHR and clinical outcomes in patients with CVD is still unclear and controversial. Consequently, in the current study, we analyzed the association of SHR and clinical outcomes in CVD patients by systematic review and meta-analysis.

MATERIALS AND METHODS: We searched the electronic databases to identify SHR studies of patients who met the eligibility criteria for CVD. We performed our study complying with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We utilized a ten terms tool to assess the potential bias of included studies. Major adverse cardiovascular and cerebrovascular events (MACCEs), all-cause death, left ventricular ejection fraction (LVEF), and other exciting outcome data were extracted for statistical analysis. Moreover, we used the DerSimonian and Laird random-effects model to perform the meta-analysis and conducted subgroup analyses to identify factors associated with substantial heterogeneity.

RESULTS: The study cohort included nine studies comprising 32,292 patients with CVD. Our meta-analysis found that MACCEs in the high SHR group were 1.68 folds compared with that in the low SHR group [odds ratio (OR) 1.68, 95% confidence interval (CI) 1.41-2.00, $p < 0.00001$]. Besides, all-cause death in the high SHR group was 1.52 folds compared with that in the low SHR group (OR 1.52, 95% CI 1.15-2.01, $p < 0.00001$). Higher SHR meant the lower LVEF (mean difference [MD] -2.03, 95% CI [-3.28-0.79], $p = 0.001$). The risk of cardiogenic shock and stroke were 2.47 and 1.53 folds in the high SHR group, respectively, compared with the low SHR group. Yet, no statistically significant difference was observed for revascularization (OR 0.88, 95% CI 0.77-1.01, $p = 0.08$), recurrent MI (OR 1.27, 95% CI 0.69-2.33, $p = 0.44$), and left ventricular end-diastolic diameter (LVEDD) (MD 0.61, 95% CI [-1.65, 2.87], $p = 0.60$) between the two groups. Subgroup analyses identified that different study design was associated with heterogeneity about MACCEs and LVEF. Besides, studies from different countries were associated with heterogeneity about all-cause death.

CONCLUSIONS: Higher SHR significantly increases the occurrence of MACCEs and all-cause death and decreases LVEF. Moreover, Higher SHR means a higher risk of cardiogenic shock and stroke. Nevertheless, SHR had no relationship with revascularization, recurrent MI, and LVEDD. As a novel and non-invasive marker, SHR should be paid more attention to in clinical practice. Future investigation should focus on the diagnostic value of SHR in CVD and the early control of stress hyperglycemia. Although no randomized, double-blind studies have been conducted, the available massive sample studies reflect the actual situation in the clinic and assist clinical decision-making.

Key Words:
Cardiovascular disease, Stress hyperglycemia ratio, Clinical outcome, Meta-analysis.

Introduction

There is no doubt that cardiovascular disease (CVD) is the leading cause of death[1]. Standardizing drug therapy and developing coronary interventional therapies have greatly reduced

Corresponding Author: Y.-W. Huang, MD; e-mail: 525654934@qq.com

CVD mortality rates[2,3]. Even so, metabolic disorders are becoming more prevalent due to excess food consumption and unhealthy lifestyles[4-6]. Stress hyperglycemia (SH), a transient elevation of blood glucose, is a strong indicator of adverse health outcomes in CVD patients[7,8]. A decreasing level of insulin and increased levels of catecholamines, steroids, and glucagon caused by stress may cause stress hyperglycemia, leading to oxidative stress and endothelial dysfunctions[9]. In this regard, critical glucose evaluations are more effective than chronic hyperglycemia status for predicting ST-segment elevation myocardial infarction (STEMI) prognoses. According to previous studies[7,10], 20-50% of patients with STEMI present with stress hyperglycemia on admission. Using a ratio of glucose and glycosylated hemoglobin (HbA1c) at admission, Roberts et al[11] developed the stress hyperglycemia ratio (SHR), which is an effective predictor of adverse events in patients with critical illnesses, according to the authors. Further, The SHR has been found to have a superior predictive value over the arterial blood gas (ABG) in cases of acute myocardial infarction (AMI) in additional studies[12,13]. Besides, several studies[14-16] have also shown that SHR can better predict in-hospital morbidity and mortality than admission glucose in patients with AMI, particularly diabetic patients. However, it has not been well-validated in patients with AMI for predicting long-term survival[12,17]. Among non-diabetic patients, Kojima et al[17] reported a positive correlation between SHR and long-term mortality, but not significantly so in the highest SHR quartile in diabetic patients. According to Singapore MI Registry data[12], SHR was an independent predictor of 1-year all-cause mortality for diabetics and non-diabetics with STEMI. Consequently, the association between SHR and clinical outcomes in patients with CVD is still unclear and controversial. In the current study, we analyzed the association of SHR and clinical outcomes in CVD patients by systematic review and meta-analysis.

Materials and Methods

We conducted the systematic review and meta-analysis of the literature specific to the study of SHR in patients with CVD, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (2020) and the Cochrane guidelines for systematic reviews of interventions[18,19]. Studies were included when inclusion criteria were met. Moreover, we registered our study with PROSPERO (https://www.crd.york.ac.uk/prospero/), and the identifier is CRD42022345587. The PRISMA 2020 checklist is presented in **Supplementary Table I**.

Literature Search Strategy

We conducted a systematic literature search of PubMed, Embase, and Cochrane Library databases. Two reviewers (Huang and Yin) comprehensively screened the electronic databases for the probable articles published from inception to the end of September 2022. Controlled vocabulary (i.e., Mesh term and Emtree) and keywords were used. The details of the search strategy are listed in **Supplementary Table II**.

Inclusion and Exclusion Criteria

Two investigators (Huang and Yin) independently estimated the studies and collected the comparative data. First, they selected all records by reading the title and abstract data. When studies were relevant, full texts were screened. We excluded all types of publications except for clinical trials and non-English studies. The investigators selected studies that met all the following criteria: (1) types of publication: articles published in peer-reviewed medical journals; (2) types of participants: CVD patients with complete data. (3) types of comparison: relative low SHR *vs.* relative high SHR; we defined the low and high SHR groups based on our previous study[20]. (4) types of outcome measure: MACCEs, all-cause death, LVEF, and other exciting outcome data (cardiogenic shock, stroke, revascularization, recurrent MI, and LVEDD).

Data Extraction

The extracted data included information on the first author's name, year of publication, country, study design, data sources, number of participants, age, rate of male, type of CVD, type of intervention, primary endpoints (MACCEs, all-cause death, LVEF), secondary endpoints (cardiogenic shock, stroke, revascularization, recurrent MI and LVEDD), clinical follow-up, and data on outcomes of interest.

Risk of Bias Assessment

The risk of bias for systematic reviews that include prospective and retrospective observational studies cannot be assessed with one tool. Hence,

we used a 10-item assessment system previously published for assessing bias risk (**Supplementary Table III**).

An evaluation system was developed to identify biases and completeness of the information. The first and second questions assessed selection bias, the third to fifth questions assessed reporting bias, the sixth question assessed attrition bias, and the seventh to tenth questions assessed the exposure. Mainly, those who answered positively, "yes," were at lower risk of bias, whereas those who responded negatively, "no," were at higher risk. Unclear or unknown risks are indicated by the term "unclear".

Statistical Analysis

We calculated odds ratios (ORs) and their corresponding 95% confidence interval (CIs) of dichotomous variables and mean differences (MDs) and their corresponding 95% CIs of continuous variables when comparing the different endpoints of low SHR group and high SHR group among CVD patients. We estimated the mean and standard deviation by the sample size, median, range, and interquartile range if the parameters were expressed as median (interquartile). The optional estimating methods were from Luo et al[21] and Wan et al[22]. The website is https://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html. Meta-analyses were performed using DerSimonian and Laird random-effects model to analyze the clinical heterogeneity[23]. We conducted subgroup analyses to identify factors associated with strong heterogeneity. $p < 0.05$ was considered statistically significant. The heterogeneity between studies was estimated using the Cochrane Q test ($p < 0.1$ or $I^2 > 50\%$ was considered to represent significant heterogeneity)[24]. All statistical analyses were conducted with Review Manager software v. 5.3.3 (Review Manager Web, The Cochrane collaboration, Copenhagen, Denmark).

Results

Result of Literature Search and Characteristics of Eligible Studies

A comprehensive literature search was performed. A total of 144 records were identified. 13 articles underwent a full-text evaluation, 4 of which were excluded (2 for inappropriate study design[15,25], and 2 for insufficient data[12,26]), leaving nine studies[16,17,27-33] in this systematic review and meta-analysis altogether. The screening process is available in a PRISMA flowchart (Figure 1). 5 studies[16,27,28,30,31] were multi- or single-center and retrospective. 4 studies[17,29,32,33] were multi- or single-center and perspective. A total of 32,292 CVD patients were included, containing 22,176 patients in the low SHR group and 10,116 patients in the high SHR group. The systematic summary is summarized in Table I.

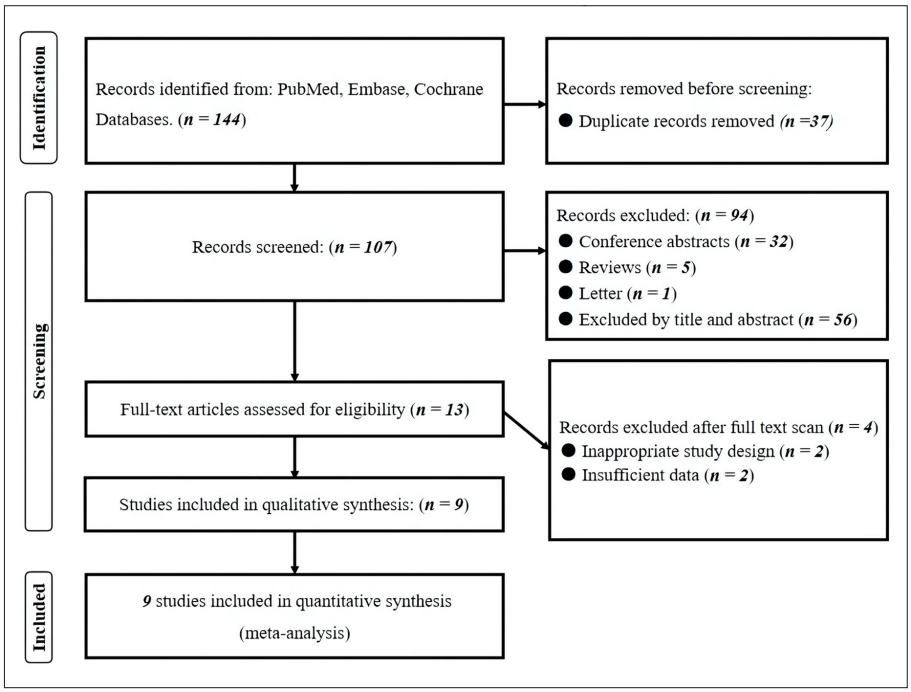

Figure 1. PRISMA flowchart of included studies.

Table I. The baseline characteristics of included studies.

Author	Year	Country	Study design	Data sources	Participants	Age (mean ± SD)	Male (%)	Type of disease	Type of intervention	Primary endpoints	Follow-up
Yang et al[28]	2017	Korea	Retrospective observational	Multi-center COACT registry	4,362	63.13 ± 10.68	65.57	CAD	PCI	MACCEs All-cause death	2.5 y (median)
Kojima et al[17]	2020	Japan	Prospective observational	Multi-center OACIS registry	6,287	65.65 ± 2.64	77.25	STEMI	—	All-cause death HF admission	5 y
Chen et al[29]	2021	China	Retrospective cohort	Single-center	341	80.70 ± 4.10	62.80	AMI	—	MACCEs All-cause death	—
Gao et al[16]	2021	China	Retrospective observational	Single-center	1,215	65.93 ± 12.13	68.15	AMI	—	AKI All-cause death	—
Meng et al[30]	2021	China	Prospective cohort	Multi-center	127	55.94 ± 11.14	86.6	ASTEMI	PCI	LVEF Ltd	6 months
Cui et al[31]	2021	China	Prospective observational	Multi-center CAMI registry	6,892	62.31 ± 12.37	76.02	AMI	—	MACCEs All-cause death	2 y
Luo et al[32]	2022	China	Retrospective observational	Multi-center NOAFCAMI-SH registry	2,089	65.70 ±12.40	76.7	AMI	—	All-cause death	2.7 y (median)
Xu et al[33]	2022	China	Retrospective observational	Multi-center	5,417	64.99 ± 2.44	69.71	ASTEMI	PCI Thrombolytic therapy	MACCEs All-cause death	30 d
Yang et al[34]	2022	China	Prospective observational cohort	Single-center	5,562	58.01 ± 10.10	76.7	ACS	Drug-eluting stent	MACCEs All-cause death	2 y

CAD: coronary artery disease; STEMI: ST-segment elevation myocardial infarction; AMI: acute myocardial infarction; ASTEMI: acute ST-segment elevation myocardial infarction; ACS: acute coronary syndrome; PCI: percutaneous coronary intervention; MACCEs: major adverse cardiovascular and cerebrovascular events; HF: heart failure; AKI: acute kidney injury; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter.

Heterogeneity, Subgroup Analyses, and Meta-Analysis of Different Outcomes

The aggregated results are presented in Table II. Our meta-analysis found that MACCEs in high SHR group was 1.68 folds compared with that in low SHR group (OR 1.68, 95% CI 1.41-2.00, $p < 0.00001$) (Figure 2A). Besides, all-cause death in the high SHR group was 1.52 folds compared with that in the low SHR group (OR 1.52, 95% CI 1.15-2.01, $p < 0.00001$) (Figure 3A). Higher SHR meant lower the LVEF (MD -2.03, 95% CI -3.28-0.79, $p = 0.001$) (Figure 4A). The risk of cardiogenic shock and stroke were 2.47 and 1.53 folds in the high SHR group, respectively, compared with the low SHR group (Figure 5A-B). Yet, no statistically significant difference was observed for LVEDD (MD 0.61, 95% CI -1.65, 2.87, $p = 0.60$) (Figure 5C), revascularization (OR 0.88, 95% CI 0.77-1.01, $p = 0.08$) (Figure 5D), and recurrent MI (OR 1.27, 95% CI 0.69-2.33, $p = 0.44$) (Figure 5E).

In the Subgroup analysis, we identified that different study design was associated with heterogeneity about MACCEs and LEVF (Figure 2B, Figure 4B). Besides, studies[16,29-34] from China were associated with heterogeneity about all-cause death (Figure 3B). Three critical outcomes had substantial heterogeneity, and we analyzed the origin of heterogeneity. Substantial heterogeneity may be the studies' diversity, the study design, or the parameter measurement tool.

Risk of Bias Assessment and Publication Bias Assessment

Based on the previous ROB assessment method, none of the analyzed studies fulfill the criteria for low risk of bias, according to the defined four sections (selection bias, reporting bias, attrition bias, exposure). Seven studies[16,17,28,29,31,33,34] could be considered at low risk for selection bias, as they consecutively enrolled patients and reported the reasons for excluding some patients from the study. All nine studies[16,17,28-34] were considered at low risk for reporting and attrition bias. Details about the ROB evaluation are reported in **Supplementary Table IV**. Publication bias assessment is presented in **Supplementary Figure 1**.

Discussion

SH is a common manifestation after stroke and AMI and strongly predicts adverse clinical outcomes[7,34-38]. The evolvement of SH may be a complicated interplay of acute physiological changes, including increased gluconeogenesis, activation of deleterious adrenergic, insulin resistance, and excessive counter-regulatory hormones, such as catecholamine, cortisol, and cytokines[39,40]. In turn, SH causes a vicious cycle and further induces inflammatory cytokines increase, oxidative stress, endothelial dysfunction, thrombosis, and

Table II. Heterogeneity, subgroup analyses, and meta-analysis of included studies.

Items		Studies, n	Results		
			OR (95% CI)	*p*-value	Heterogeneity (I^2, *p* for Cochran Q)
MACCEs	Prospective	2	1.43 (1.30, 1.58)	$p < 0.00001$	$I^2 = 0\%$, $p = 0.59$
	Retrospective	3	1.92 (1.57, 2.36)	$p < 0.00001$	$I^2 = 56\%$, $p = 0.0008$
	Pooled	5	1.68 (1.41, 2.00)	$p < 0.00001$	$I^2 = 79\%$, $p = 0.0008$
All-cause death	China	6	1.72 (1.14, 2.60)	$p = 0.010$	$I^2 = 94\%$, $p < 0.00001$
	Non-China	2	1.60 (1.38, 1.87)	$p < 0.00001$	$I^2 = 0\%$, $p = 0.59$
	Pooled	8	1.67 (1.25, 2.23)	$p = 0.0005$	$I^2 = 91\%$, $p < 0.00001$
	Cardiogenic shock	2	2.47 (1.44, 4.23)	$p = 0.001$	$I^2 = 54\%$, $p = 0.14$
	Stroke	3	1.53 (1.11, 2.12)	$p = 0.010$	$I^2 = 0$, $p = 0.52$
	Revascularization	2	0.88 (0.77, 1.01)	$p = 0.08$	$I^2 = 0$, $p = 0.92$
	Recurrent MI	3	1.27 (0.69, 2.33)	$p = 0.44$	$I^2 = 54\%$, $p = 0.12$
			MD (95% CI)	*p*-value	Heterogeneity (I^2, *p* for Cochran Q)
LVEF	Prospective	4	-2.27 (-3.83, -0.71)	$p = 0.004$	$I^2 = 98\%$, $p < 0.00001$
	Retrospective	2	-1.58 (-2.52, -0.63)	$p = 0.001$	$I^2 = 0\%$, $p = 0.50$
	Pooled	6	-2.03 (-3.28, -0.79)	$p = 0.001$	$I^2 = 97\%$, $p < 0.00001$
LVEDD		2	0.61 (-1.65, 2.87)	$p = 0.60$	$I^2 = 83\%$, $p = 0.01$

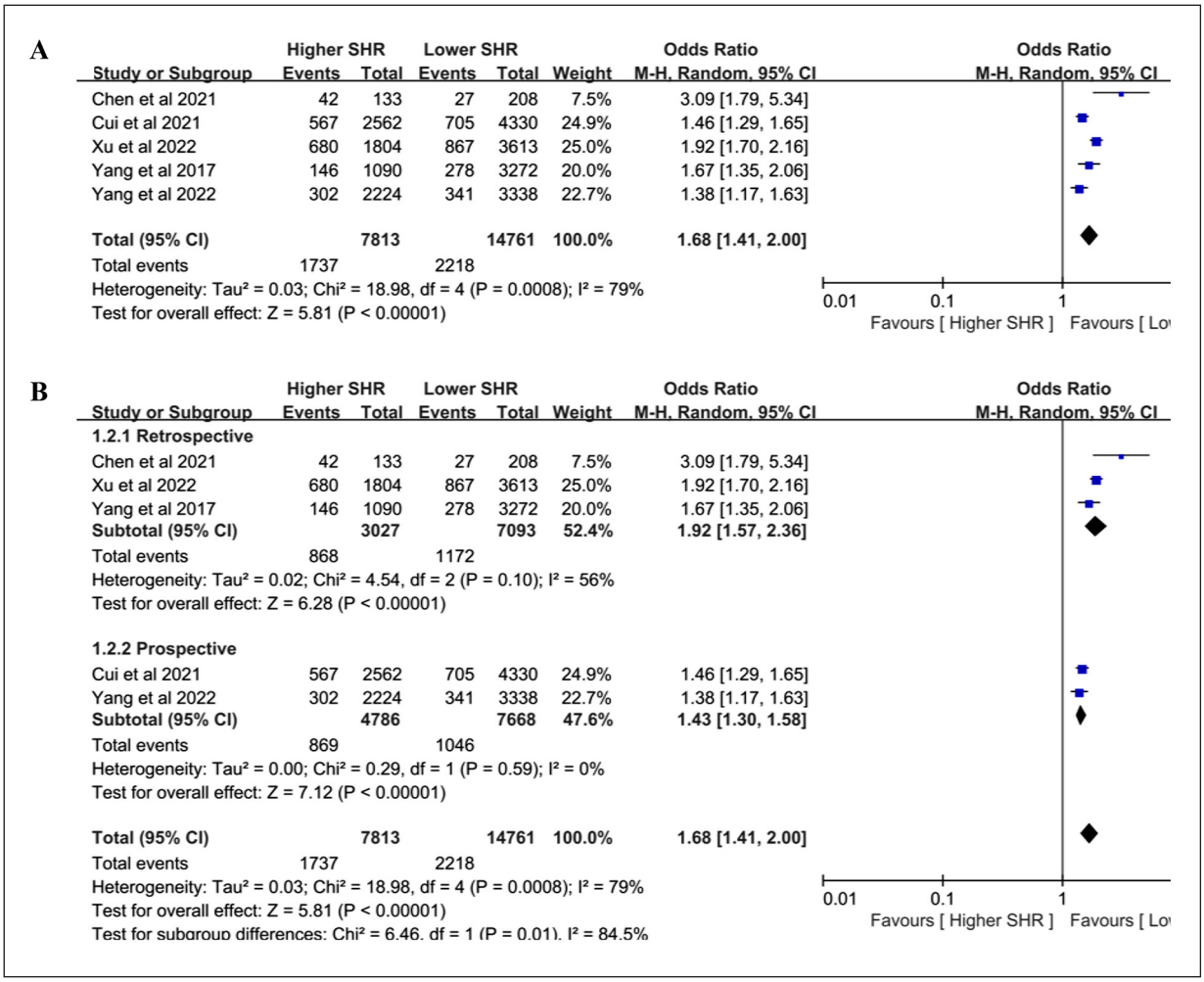

Figure 2. The MACCEs (**A**), subgroup analysis of MACCEs between higher SHR and lower SHR group (**B**).

ischemia-reperfusion injury, all of which could cause further cardiac damage[41-44]. As a result, higher SHR may reflect the severe changes in AMI patients about the inflammatory, and hemodynamic status, particularly in those with severe complications such as cardiogenic shock or infection. Besides, acute fluctuations in glucose levels are associated with increased plaque instability, infarct size, and worse heart function[45]. Recent studies[8,25] found that SH was strongly related to intracoronary thrombus burden and no-reflow phenomenon, which may explain the higher mortality risk and cardiogenic shock in the high SHR group.

A study from Yang et al[27] showed that SHR is a useful predictive marker of MACCE in non-diabetic patients with STEMI undergoing percutaneous coronary intervention (PCI). This non-invasive parameter could be used to identify high-risk patients for poor outcomes. Another study[17] demonstrated that high SHR was significantly associated with worse long-term prognosis in STEMI patients without diabetes mellitus. However, the association between SHR and long-term outcomes in non-diabetic patients with STEMI requires more prospective studies. Chen et al[28] showed that SHR is a simple and robust predictor of in-hospital outcomes in elderly, non-diabetic patients with AMI. Gao et al[16] focused on diabetic patients and found that the SHR is a better predictor of in-hospital mortality and morbidity in AMI patients than admission glycemia. Meng et al[29] initiated a new study about left ventricular remodeling, explaining that SHR is significantly associated with adverse left ventricular remodeling after STEMI.

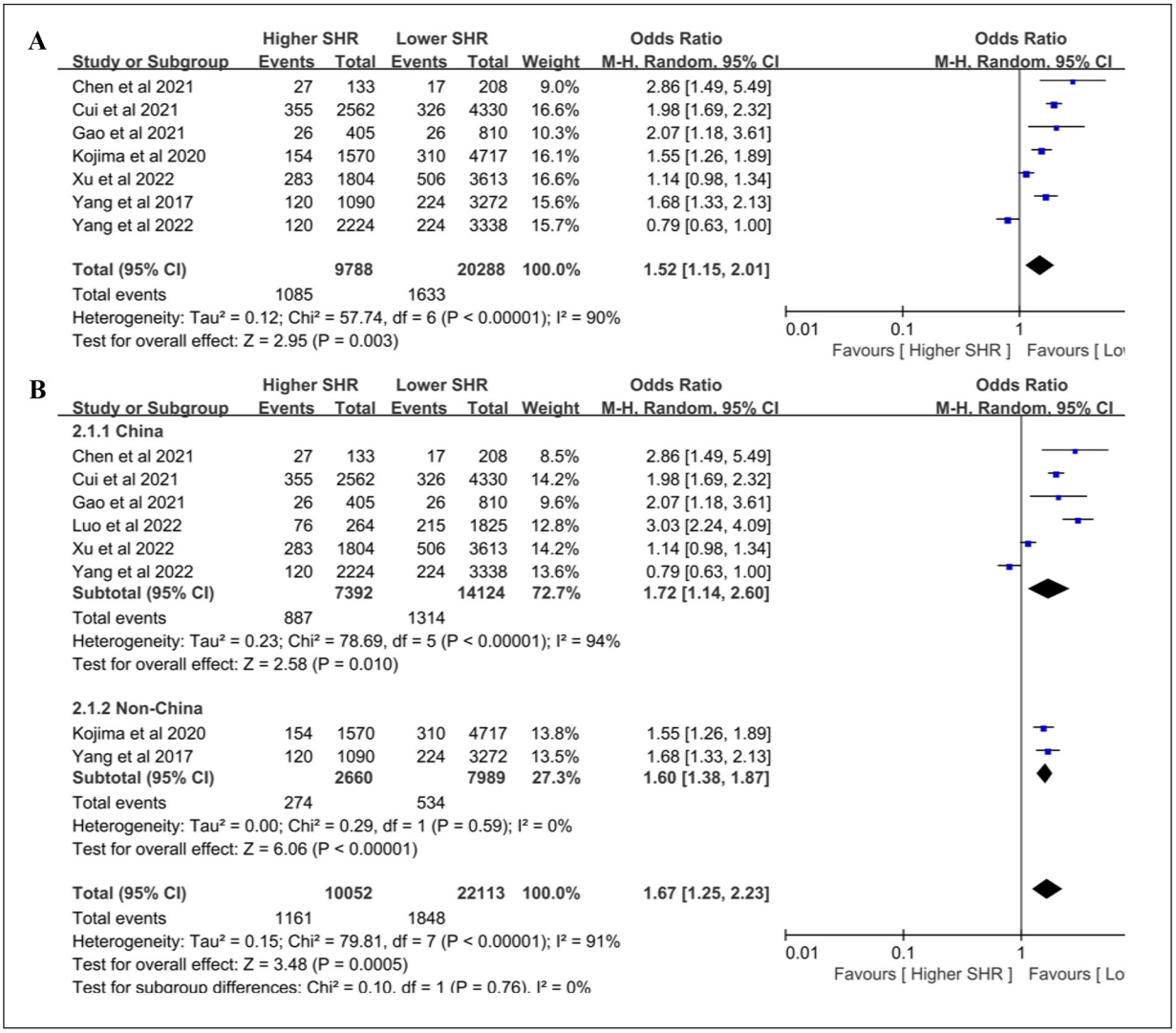

Figure 3. The All-cause death (**A**), subgroup analysis of All-cause death between higher SHR and lower SHR group (**B**).

Nevertheless, future studies with large sample sizes are still warranted. A study conducted by Cui et al[30] showed that no matter whether patients with or without diabetes, a strong positive association between SHR and long-term mortality in patients with AMI existed. In other words, SHR could be considered a valuable marker for risk stratification in these patients because it is widely available, non-invasive, and relatively inexpensive[29,30]. Compared with the Global Registry of Acute Coronary Events (GRACE) score, The accuracy of SHR for predicting long-term mortality is much higher, which indicates the potential of SHR as a biomarker for post-MI risk stratification among diabetic patients[31]. In 2022, a massive sample and multi-center study[32] including 7,476 acute STEMI patients was performed by Xu et al[32]. Their findings showed that SHR is independently related to the risks of MACCEs and mortality in patients with STEMI. Significantly, SHR may help improve the predictive efficacy of the thrombolysis in myocardial infarction (TIMI) risk score in diabetic patients with STEMI. Another study from China focused on patients with the acute coronary syndrome. They found U-shaped associations in MACCEs and J-shaped associations in in-hospital cardiac death and MI. All acute coronary syndrome (ACS) patients who underwent drug-eluting stent implantation underwent a 2-year follow-up, and the cutoff value of SHR for poor prognosis was 0.78[33].

Our meta-analysis has systematically reviewed the current studies that compared different SHRs in CVD patients with/without diabetes, and we

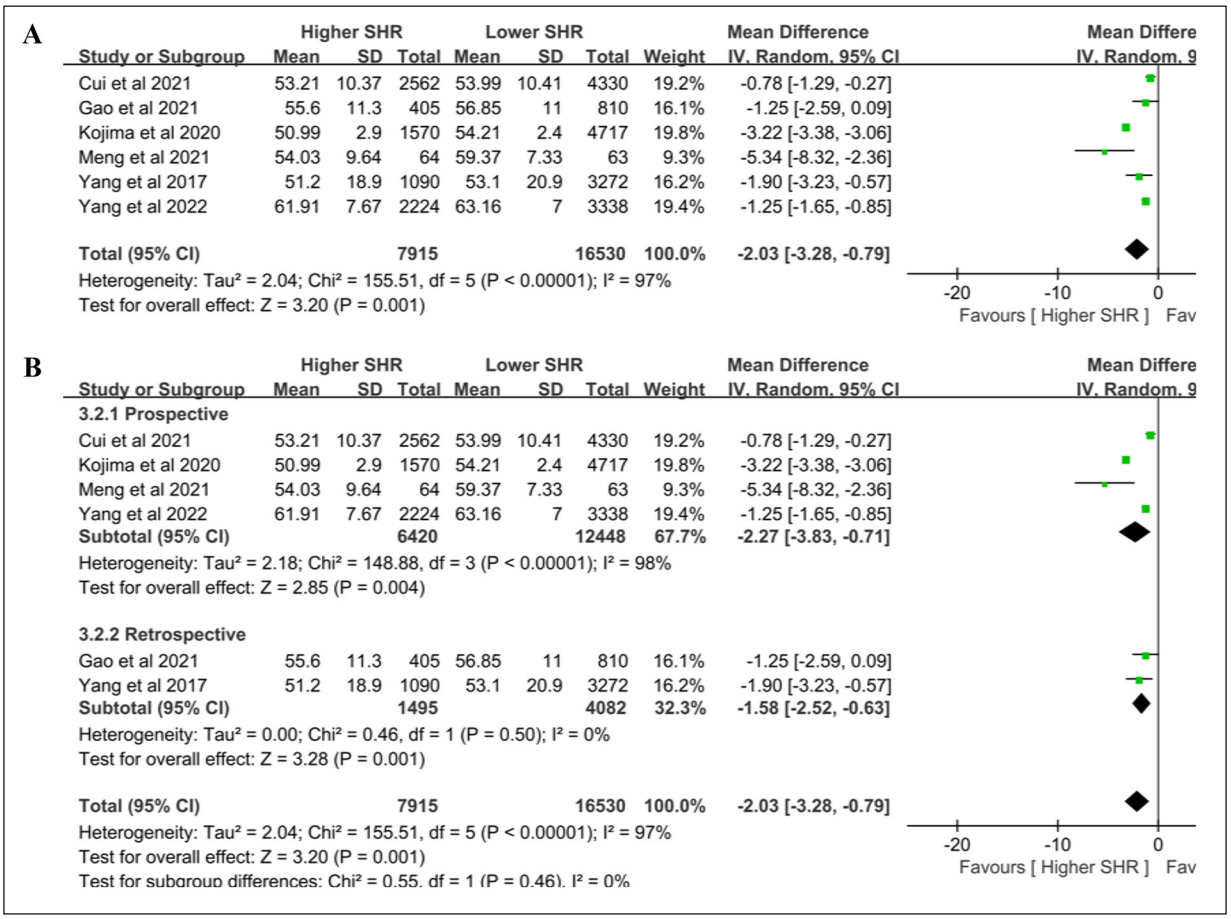

Figure 4. The LVEF (**A**), Subgroup analysis of LVEF between higher SHR and lower SHR group (**B**).

obtained three significant findings. First, in patients with CVD, higher SHR indicated a higher rate of MACCEs and all-cause death. Higher SH meant lower LVEF, which reflects cardiac function. Second, high SHR was also related to cardiogenic shock and stroke, but the studies are limited. Third, the relationship between SHR and myocardial markers (CK, CK-MB, cTnI) is unclear, and relevant studies are warranted. Forth, only one study[30] systematically investigated cardiac function. Hence the correlative studies are urgent. By appraising SHR, earlier identification of the adverse results, such as deadly MI, is vital for the cardiologist.

Limitations

Our study has some limitations: first, all studies are mainly retrospective and prospective studies rather than randomized controlled trials, even though most of the studies are multi-center and massive samples; second, seven studies[16,29-34] were from Chinese scholars, and only two studies[17,28] were from another country (Japan and Korea). Besides, no study from Occident was included. Hence, more studies from Occident and other races are required. Third, substantial heterogeneity may affect the robustness of our findings. Fourth, few studies focus on cardiac function parameters and myocardial markers. When PCI was performed, myocardial perfusion should be considered between the high SHR group and the low SHR group. Further studies should concentrate on these aspects. Despite these limitations, we believe that the preliminary findings of our meta-analysis may be helpful to clinicians in their choice of SH treatment for CVD patients.

Conclusions

Higher SHR significantly increases the occurrence of MACCEs and all-cause death and decreases LVEF, reflecting cardiac function. Moreover, Higher SHR means a higher risk of cardio-

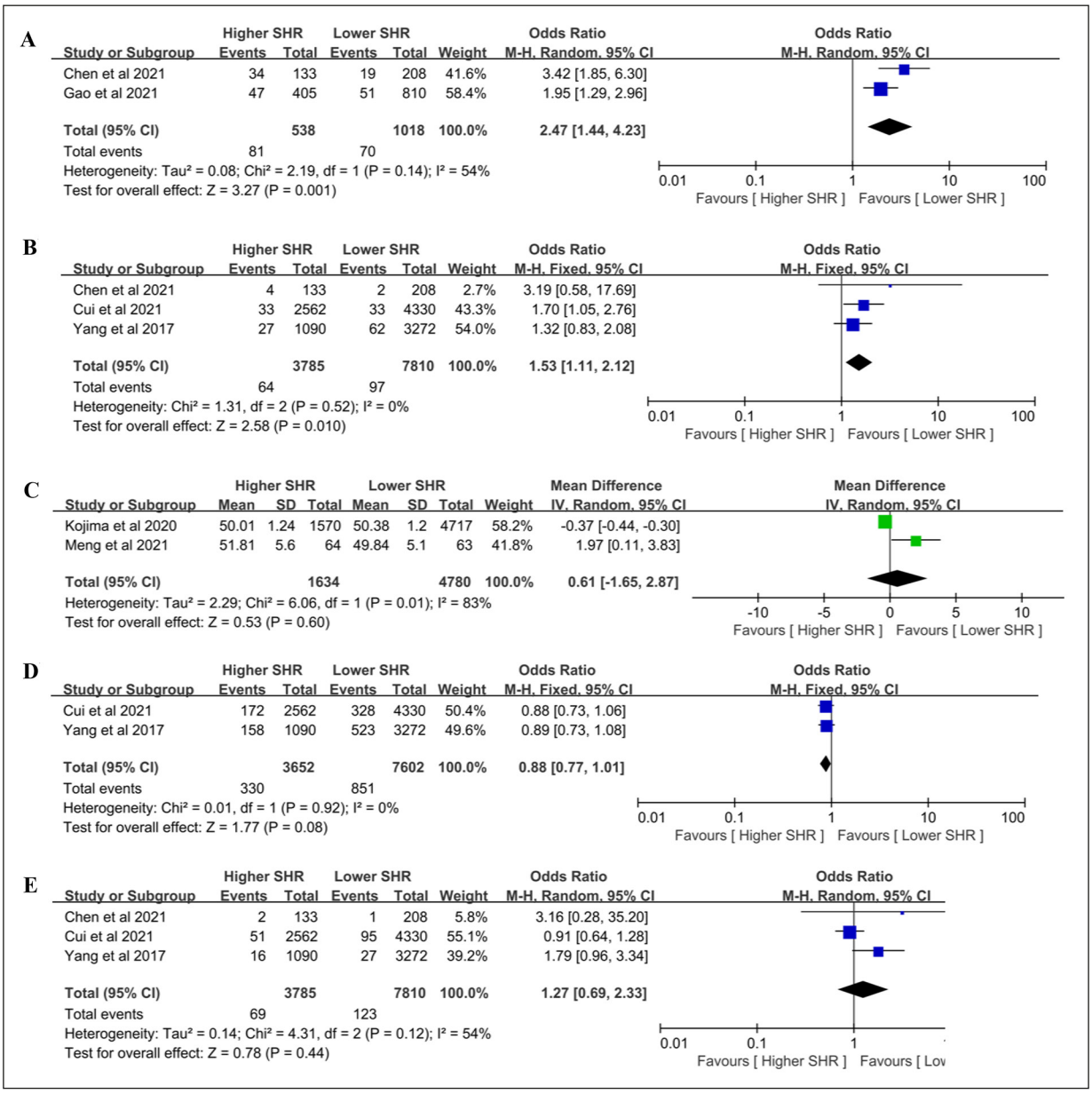

Figure 5. The cardiogenic shock (**A**), stroke (**B**), LVEDD (**C**), revascularization (**D**), and recurrent MI between higher SHR and lower SHR group (**E**).

genic shock and stroke. Nevertheless, SHR had no relationship with revascularization, recurrent MI, and LVEDD. As a novel and non-invasive marker, SHR should be paid more attention to in clinical practice. Future investigation should focus on the diagnostic value of SHR in CVD and the early control of stress hyperglycemia. Although no randomized, double-blind studies have been conducted, the available massive sample studies reflect the actual situation in the clinic and assist clinical decision-making.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Availability of Data and Materials

The original contributions presented in the study are included in the article or in Supplementary Materials; further inquiries can be directed to the corresponding author.

Ethics Approval

Not applicable.

Authors' Contribution

TY.-W. Huang and X.-S Yin developed the initial idea for this study. Y.-H An and Z.-P. Li developed and revised the search strategy. Y.-W. Huang and X.-S Yin contributed to the original draft. Z.-P. Li was responsible for the revision of the draft. Y.-W. Huang, Y.-H An, and X.-S Y in contributed equally and are co-first authors. All authors approved the final version of the manuscript before submission.

Funding

Not applicable.

Trial Registration

Systematic review registration: https://www.crd.york.ac.uk/prospero/, identifier: CRD 42022345587.

References

1) Sacco RL, Roth GA, Reddy KS, Arnett DK, Bonita R, Gaziano TA, Heidenreich PA, Huffman MD, Mayosi BM, Mendis S, Murray CJ, Perel P, Piñeiro DJ, Smith SC Jr, Taubert KA, Wood DA, Zhao D, Zoghbi WA. The Heart of 25 by 25: achieving the goal of reducing global and regional premature deaths from cardiovascular diseases and stroke: a modeling study from the American Heart Association and World Heart Federation. Circulation 2016; 133: e674-690.
2) Leong DP, Joseph PG, McKee M, Anand SS, Teo KK, Schwalm JD, Yusuf S. Reducing the global burden of cardiovascular disease, part 2: prevention and treatment of cardiovascular disease. Circ Res 2017; 121: 695-710.
3) Bhatnagar P, Wickramasinghe K, Wilkins E, Townsend N. Trends in the epidemiology of cardiovascular disease in the UK. Heart 2016; 102: 1945-1952.
4) Saklayen MG. The global epidemic of the metabolic syndrome. Curr Hypertens Rep 2018; 20: 12.
5) Wang Y, Mi J, Shan XY, Wang QJ, Ge KY. Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. Int J Obes 2007; 31: 177-188.
6) Rodríguez-Monforte M, Sanchez E, Barrio F, Costa B, Flores-Mateo G. Metabolic syndrome and dietary patterns: a systematic review and meta-analysis of observational studies. Eur J Nutr 2017; 56: 925-947.
7) Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 2000; 355: 773-778.
8) Khalfallah M, Abdelmageed R, Elgendy E, Hafez YM. Incidence, predictors and outcomes of stress hyperglycemia in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention. Diab Vasc Dis Res 2020; 17: 1479164119883983.
9) Qaseem A, Humphrey LL, Chou R, Snow V, Shekelle P, Clinical Guidelines Committee of the American College of Physicians. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2011; 154: 260-267.
10) Wahab NN, Cowden EA, Pearce NJ, Gardner MJ, Merry H, Cox JL, ICONS Investigators. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002; 40: 1748-1754.
11) Roberts GW, Quinn SJ, Valentine N, Alhawassi T, O'Dea H, Stranks SN, Burt MG, Doogue MP. Relative hyperglycemia, a marker of critical illness: introducing the stress hyperglycemia ratio. J Clin Endocrinol Metab 2015; 100: 4490-4497.
12) Sia CH, Chan MH, Zheng H, Ko J, Ho AF, Chong J, Foo D, Foo LL, Lim PZ, Liew BW, Chai P, Yeo TC, Tan HC, Chua T, Chan MY, Tan JWC, Bulluck H, Hausenloy DJ. Optimal glucose, HbA1c, glucose-HbA1c ratio and stress-hyperglycaemia ratio cut-of values for predicting 1-year mortality in diabetic and non-diabetic acute myocardial infarction patients. Cardiovasc Diabetol 2021; 20: 211.
13) Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefned-a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefnition of myocardial infarction. J Am Coll Cardiol 2000; 36: 959-969.
14) Marenzi G, Cosentino N, Milazzo V, Metrio MD, Cecere M, Mosca S, Rubino M, Campodonico J, Moltrasio M, Marana I, Grazi M, Lauri G, Bonomi A, Veglia F, Manfrini R, Bartorelli AL. Prognostic value of the acute-to-chronic glycemic ratio at admission in acute myocardial infarction: a prospective study. Diabetes Care 2018; 41: 847-853.
15) Lee TF, Burt MG, Heilbronn LK, Mangoni AA, Wong VW, McLean M, Cheung NW. Relative hyperglycemia is associated with complications following an acute myocardial infarction: a post-hoc analysis of HI-5 data. Cardiovasc Diabetol 2017; 16: 157.
16) Gao SD, Liu QB, Ding XS, Chen H, Zhao XQ, Li HW. Predictive value of the acute-to-chronic glycemic ratio for in-hospital outcomes in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. Angiology 2020; 71: 38-47.
17) Kojima T, Hikoso S, Nakatani D, Suna S, Dohi T, Mizuno H, Okada K, Kitamura T, Kida H, Oeun B, Sunaga A, Kurakami H, Yamada T, Sakata Y, Sato H, Hori M, Komuro I, Sakata Y. Impact of hyper-

glycemia on long-term outcome in patients with ST-segment elevation myocardial infarction. Am J Cardiol 2020; 125: 851-859.

18) Higgins JP, Green S. (Eds.) Cochrane Handbook for Systematic Reviews of Interventions 2010: 485-488.

19) Huang YW, Yin XS, Li ZP. Association of the stress hyperglycemia ratio and clinical outcomes in patients with cardiovascular diseases: a systematic review and meta-analysis. Front Neurol 2022; 13: 999536.

20) Huang YW, Yin XS, Li ZP. Association of the stress hyperglycemia ratio and clinical outcomes in patients with stroke: a systematic review and meta-analysis. Front Neuro 2022; 13: 999536.

21) Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range and/or mid-quartile range. Stat Methods Med Res 2018; 27: 1785-1805.

22) Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014; 14: 135.

23) DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177-188.

24) Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002; 21: 1539-1558.

25) Chu JP, Tang JN, Lai Y, Gao YH, Ye Z, Guan CY, Ding KK, Yao Y, Chen F, Liu XB. Association of stress hyperglycemia ratio with intracoronary thrombus burden in diabetic patients with ST-segment elevation myocardial infarction. J Thorac Dis 2020; 12: 6598-6608.

26) Schmitz T, Freuer D, Harmel E, Heier M, Peters A, Linseisen J, Meisinger C. Prognostic value of stress hyperglycemia ratio on short- and long-term mortality after acute myocardial infarction. Acta Diabetol 2022; 59: 1019-1029.

27) Yang Y, Kim TH, Yoon KH, Chung WS, Ahn Y, Jeong MH, Seung KB, Lee SH, Chang K. Stress hyperglycemia ratio, an index of relative hyperglycemia, as a predictor of clinical outcomes after percutaneous coronary intervention. Int J Cardiol 2017; 241: 57-63.

28) Chen G, Li M, Wen X, Wang R, Zhou Y, Xue L, He X. Association Between Stress Hyperglycemia Ratio and In-hospital Outcomes in Elderly Patients With Acute Myocardial Infarction. Front Cardiovasc Med 2021; 8: 698725.

29) Meng S, Zhu Y, Liu K, Jia R, Nan J, Chen M, Lei X, Zou K, Jin Z. The stress hyperglycaemia ratio is associated with left ventricular remodelling after first acute ST-segment elevation myocardial infarction. BMC Cardiovasc Disord 2021; 21: 72.

30) Cui K, Fu R, Yang J, Xu H, Yin D, Song W, Wang H, Zhu C, Feng L, Wang Z, Wang Q, Lu Y, Dou K, Yang Y, CAMI Registry Investigators. Stress hyperglycemia ratio and long-term mortality after acute myocardial infarction in patients with and without diabetes: A prospective, nationwide, and multicentre registry. Diabetes Metab Res Rev 2022; 38: e3562.

31) Luo J, Xu S, Li Z, Gong M, Qin X, Zhang X, Hao C, Liu X, Zhang W, Xu W, Liu B, Wei Y. Prognostic impact of stress hyperglycemia ratio in acute myocardial infarction patients with and without diabetes mellitus. Nutr Metab Cardiovasc Dis 2022; 32: 2356-2366.

32) Xu W, Yang YM, Zhu J, Wu S, Wang J, Zhang H, Shao XH. Predictive value of the stress hyperglycemia ratio in patients with acute ST-segment elevation myocardial infarction: insights from a multi-center observational study. Cardiovasc Diabetol 2022; 21: 48.

33) Yang J, Zheng Y, Li C, Gao J, Meng X, Zhang K, Wang W, Shao C, Tang YD. 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: 947-956.

34) Dungan KM, Braithwaite SS, Preiser JC. Stress hyperglycaemia. Lancet 2009; 373: 1798-1807.

35) Melamed E. Reactive hyperglycaemia in patients with acute stroke. J Neurol Sci 1976; 29: 267-275.

36) Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. Mayo Clin Proc 2003; 78: 1471-1478.

37) Kim EJ, Jeong MH, Kim JH, Ahn TH, Seung KB, Oh DJ, Kim HS, Gwon HC, Seong IW, Hwang KK, Chae SC, Kim KB, Kim YJ, Cha KS, Oh SK, Chae JK, KAMIR-NIH registry investigators. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients. Int J Cardiol 2017; 236: 9-15.

38) Ishihara M, Kojima S, Sakamoto T, Kimura K, Kosuge M, Asada Y, Kim HS, Gwon HC, Seong IW, Hwang KK, Chae SC, Kim KB, Kim YJ, Cha KS, Oh SK, Chae JK, KAMIR-NIH registry investigators. Comparison of blood glucose values on admission for acute myocardial infarction in patients with versus without diabetes mellitus. Am J Cardiol 2009; 104: 769-774.

39) Lazzeri C, Valente S, Chiostri M, Picariello C, Gensini GF. Acute glucose dysmetabolism in the elderly with ST elevation myocardial infarction submitted to mechanical revascularization. Int J Cardiol 2012; 155: 66-69.

40) Huberlant V, Preiser JC. Year in review 2009: critical care-metabolism. Crit Care 2010; 14: 238.

41) Ray KK, Cannon CP, Morrow DA, Kirtane AJ, Buros J, Rifai N, McCabe CK, Gibson CM, Braunwald E. Synergistic relationship between hyperglycaemia and inflammation with respect to clinical outcomes in non-ST-elevation acute coronary syndromes: analyses from OPUS-TIMI 16 and TACTICS-TIMI 18. Eur Heart J 2007; 28: 806-813.

42) Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP, Colette C. Activation of oxida-

tive stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA 2006; 295: 1681-1687.

43) Ceriello A, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R, Boemi M, Giugliano D. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes 2008; 57: 1349-1354.

44) Worthley MI, Holmes AS, Willoughby SR, Kucia AM, Heresztyn T, Stewart S, Chirkov YY, Zeitz CJ, Horowitz JD. The deleterious effects of hyperglycemia on platelet function in diabetic patients with acute coronary syndromes mediation by superoxide production, resolution with intensive insulin administration. J Am Coll Cardiol 2007; 49: 304-310.

45) Ujueta F, Weiss EN, Sedlis SP, Shah B. Glycemic control in coronary revascularization. Curr Treat Options Cardiovasc Med 2016; 18: 12.