

THE ASSOCIATION BETWEEN STRESS HYPERGLYCEMIA RATIO (SHR) AND CARDIOVASCULAR EVENT IN ACUTE CORONARY SYNDROME PATIENTS AT ADAM MALIK HOSPITAL

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ABSTRACT

Introduction: Acute hyperglycemia in patients with acute coronary syndrome (ACS) has been associated with major adverse cardiovascular events (MACE). The stress hyperglycemia ratio (SHR) is considered a potential marker for predicting MACE in ACS patients. This study aims to evaluate the relationship between SHR and MACE among ACS patients at Adam Malik Hospital, Medan. **Methods:** This study employed a retrospective analytic design by collecting data from the medical records of ACS patients treated at Adam Malik Hospital, Medan, during 2022–2023. Inclusion criteria included: confirmed ACS patients (who underwent coronary angiography), while exclusion criteria were: patients with an E-GFR <30 ml/min and those with malignancies, liver diseases, hematological disorders, or infections (sepsis). The chi-square test was used to evaluate the relationship between variables, with a p-value <0.05 considered statistically significant.

Results: A total of 100 ACS patients met the study criteria, with an average age of 59 ± 10.3 years, and 78% were male. The mean SHR among the study subjects was 1.09 ± 0.36 . MACE was recorded in 64% of patients, including heart failure in 44%, rehospitalization in 12%, stroke in 9%, and mortality in 31%. SHR was found to have a significant relationship with overall MACE ($p < 0.001$) and heart failure events ($p = 0.001$). However, no association was found between SHR and stroke, rehospitalization, mortality, or 3-point MACE ($p > 0.05$).

Conclusion: SHR has a significant relationship with MACE but not with 3-point MACE.

Keywords: acute coronary syndrome, stress hyperglycemia ratio, major adverse cardiovascular events, acute hyperglycemia

ABSTRAK

Latar Belakang: Hiperglikemia akut yang terjadi pada pasien dengan sindrom koroner akut (SKA) telah dikaitkan dengan kejadian kardiovaskular mayor (KKM). Stress Hyperglycemia Ratio (SHR) dianggap sebagai marker potensial yang dapat memprediksi KKM pada pasien SKA. Penelitian ini bertujuan untuk menilai hubungan SHR dengan KKM pada pasien SKA di RS Adam Malik Medan.

Metode: Penelitian ini menggunakan desain retrospektif analitik dengan pengumpulan data dari rekam medis pasien SKA yang dirawat di RS Adam Malik Medan selama tahun 2022 - 2023. Kriteria inklusi termasuk: pasien yang terkonfirmasi dengan SKA (menjalani prosedur angiografi koroner), sedangkan untuk kriteria eksklusi yaitu: pasien dengan E-GFR <30 ml/min dan mempunyai penyakit keganasan, penyakit hepar, kelainan darah, dan infeksi (sepsis). Uji chi-square digunakan untuk menilai hubungan antar variabel. Nilai $p < 0,05$ dianggap bermakna secara statistik.

Hasil: Terdapat sebanyak 100 penderita SKA yang memenuhi kriteria penelitian, dengan rerata usia penderita $59 \pm 10,3$ tahun dan laki-laki sebanyak 78%. Rerata SHR pada subjek penelitian yaitu $1,09 \pm 0,36$. Kejadian KKM tercatat pada 64%



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pasien, dengan kasus gagal jantung sebanyak 44%, rehospitalisasi 12%, stroke 9%, dan kematian 31%. SHR ditemukan mempunyai hubungan signifikan dengan KKM secara keseluruhan ($p < 0,001$) dan kejadian gagal jantung ($p = 0,001$). Namun, tidak ditemukan hubungan antara SHR dengan kejadian stroke, reshospitalisasi, kematian, dan KKM 3 poin ($p > 0,05$).

Kesimpulan: *SHR mempunyai hubungan yang signifikan terhadap KKM, tetapi tidak terdapat hubungan terhadap KKM 3 poin.*

Keyword: *Sindrom Koroner Akut, Stress Hyperglycemia Ratio, Kejadian Kardiovaskular Mayor, Hiperglikemia akut*

1. Introduction

Acute Coronary Syndrome (ACS) is a leading cause of death worldwide, despite the development of prevention and treatment strategies. Metabolic disorders, including hyperglycemia, insulin resistance, and dyslipidemia caused by unhealthy lifestyles, lead to the increasing prevalence of ACS[1,2].

World Health Organization (WHO) data estimates that 17.9 million people died from cardiovascular disease in 2019, contributing 32% of global deaths. Riskesdas data in 2018 showed that the prevalence of cardiovascular disease in Indonesia reached 1.5%, 15 out of 1000 people, or there were 4.2 million people suffering from cardiovascular disease, with the prevalence of heart disease reaching 1.3% in North Sumatra[3,4,5].

Major adverse cardiovascular events (MACE) does not have a concrete definition, but over time, various definitions have been used in cardiovascular research with MACE selected as the primary or secondary endpoint. The components of MACE are heart failure, non-fatal re-infarction, recurrent angina, re-hospitalization for cardiovascular-related diseases, recurrent Primary Cutaneous Intervention (PCI), Coronary Artery Bypass Graft (CABG), unscheduled coronary revascularization, stroke, re-infarction, and all-cause death and mortality. The components of MACE include cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke[6,7]. Hyperglycemia contributes to MACE through mechanisms such as endothelial dysfunction caused by oxidative stress, chronic inflammation from cytokine release, and metabolic dysregulation leading to myocardial injury and atherosclerosis. These factors collectively increase the risk of adverse cardiovascular outcomes.

Chronic hyperglycemia caused by Diabetes Mellitus (DM) is a well-known risk factor for adverse cardiovascular outcomes. Stress Hyperglycemia, a transient increase in blood glucose, is a strong indicator of adverse prognosis in CHD patients. Stress-induced decreases in insulin levels and increases in catecholamine, steroid, and glucagon levels can lead to stress hyperglycemia, which leads to oxidative stress and endothelial dysfunction. In this regard, critical glucose is more effective than chronic hyperglycemia in predicting ACS events[8,9].

Stress Hyperglycemia Ratio (SHR) represents relative hyperglycemia and has been shown to be effective in predicting worsening prognosis in patients with severe acute illness, including patients with ACS[1,2]. SHR has been found to have superior predictive value compared to Arterial Blood Gas Analysis (ABGA) in cases of Acute Myocardial Infarction (AMI). Other studies have also suggested that SHR can better predict in-hospital morbidity and mortality compared to admission glucose in patients with AMI[8,10].

This studied relationships may be a comprehensive effect of a heterogeneous population with ACS. Therefore, it is necessary to further assess this relationship in certain conditions. Studies on the relationship between SHR and mortality in patients with ACS are still limited. Therefore, researchers want to know whether there is a relationship between Stress Hyperglycemia Ratio (SHR) and Major Adverse Cardiovascular Events (MACE) in Acute Coronary Syndrome (ACS) Patients at Adam Malik Hospital Medan.

2. Research Method

This research is an observational analytical study with retrospective design and uses data collection from secondary medical records to assess the relationship between Stress Hyperglycemia Ratio (SHR) and Major Adverse Cardiovascular Events (MACE) in Acute Coronary Syndrome (ACS) Patients at Adam Malik Hospital, Medan. The study was conducted at Adam Malik Hospital using inpatient medical record data after obtaining approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (FK USU). The research will be carried out within a specific timeframe, and data will be collected from February 2023 until May 2024.

The sampling technique in this study was consecutive sampling, sample determination was carried out with certain considerations, namely inclusion criteria and exclusion criteria. Inclusion criteria included patients with clinical and examinations that supported ACS (based on clinical, ECG and cardiac biomarkers) and ACS patients who underwent coronary angiography procedures during hospitalization. Exclusion criteria included patients with E-GFR < 30 ml/min, incomplete medical record data, and patients with malignant diseases, liver disease, blood disorders and infections (sepsis).

In this study, researchers chose Stress Hyperglycemia Ratio (SHR) in ACS patients as the independent variable, and Major Cardiovascular Events (MACE) in ACS patients as the dependent variable. MACE itself is defined as

death due to cardiovascular causes, stroke, hospitalization/revascularization, and heart failure. Secondary data collection including demographic and clinical information, as well as Major Cardiovascular Events (MACE, including cardiovascular death, stroke, rehospitalization, heart failure), Major Cardiovascular Events 3 Points (MACE 3 Points, including death due to cardiovascular causes, myocardial infarction and stroke), and Acute Coronary Syndrome (ACS) were then obtained from the medical records. Stress Hyperglycemia Ratio (SHR) were obtained from calculations of random blood sugar with HbA1c (GDS (mmol/L) / $[1.59 \times \text{HbA1c}(\%) - 2.59]$).

Descriptive statistical analysis was used for demographic data. Analytical statistical analysis with chi square was used to test the categorical variable of SHR in the MACE group. The research data were analyzed statistically with the help of the Windows SPSS (Statistical Product and Science Service) version 25.0 computer program. Differences were considered statistically significant if $p < 0.05$. Furthermore, to determine the strength of the relationship between independent and dependent variables, the Spearman rank test will be used. All analyses will be conducted using SPSS (Statistical Product and Service Solutions) software.

3. Results

This study has been conducted at Adam Malik Hospital with the approval of the Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara (FK USU). The research and data collection were carried out through the medical records of inpatient patients from Februari 2023 until May 2024. The study was conducted using a cross-sectional method, and the design was based on consecutive sampling. A total of 100 samples were used in this study.

Table 1 Research Data Characteristic

Parameter	<i>n</i> = 100
Age (year)	
<50	18 (18%)
50-59	40 (40%)
≥60	42 (42%)
Mean ± SD	59 ± 10,3
Gender <i>n</i> (%)	
Male	78 (78%)
Female	22 (22%)
Stroke	
Yes	9 (9%)
No	91 (91%)
Heart Failure	
Yes	44 (44%)
No	56 (56%)
Rehospitalization/Revascularization	
Yes	12 (12%)
No	88 (88%)
Mortality	
Yes	31 (31%)
No	69 (69%)
MACE	
Yes	64 (64%)
No	36 (36%)
MACE 3 Points	
Yes	9 (8.9%)
No	91 (90.1%)
GDS (mg/dl)	
Mean ± SD	190 ± 10,3 mg/dl
Hba1c (%)	
Mean ± SD	7,81 ± 2,78
SHR	
<0.98	39 (39%)
>0.98 s/d 1.32	40 (40%)
>1.32	21 21%)

Based on Table 1 regarding the characteristics of the study samples below, out of a total of 100 samples, the average age of the study participants was 59 + 10.3 years. Regarding gender characteristics, there are 78 individuals (78.0%)

who are male and 22 individuals (22.0%) who are female. There were nine patients with stroke (9%), 44 patients with heart failure (44%), 12 patients with rehospitalization/revascularization (12%), 31 deaths caused by heart failure (33%). In this study, the case number of MACE is 64 (64%), MACE 3 points is 9 (8.9%). The average initial fasting blood glucose level on admission to the hospital examined in this study was 190 ± 10.3 mg/dl, with average HbA1c is 7.81 ± 2.78 . SHR values <0.98 were found by 39 people (39%), >0.98 to 1.32 by 40 people (40%), and >1.32 were found by 21 people (21%).

Table 2 SHR with heart failure

SHR	Heart Failure				P value
	Yes		No		
	n	%	n	%	
<0.98	7	7%	32	32%	0,001
>0.98 s/d 1.32	24	24%	16	16%	
>1.32	13	13%	8	8%	

In table 2, related to the relationship between SHR and heart failure statistically using the chi square test, it was found that there was a relationship between SHR and heart failure at Adam Malik Hospital with a p value = 0.001 ($p < 0.05$).

Table 3 SHR with stroke

SHR	Stroke				P value
	Yes		No		
	n	%	n	%	
<0.98	1	1%	38	38%	0,193
>0.98 s/d 1.32	5	5%	35	35%	
>1.32	3	3%	18	18%	

In table 3, related to the relationship between SHR and stroke statistically with the chi square test or fischer exact test, the value of $p = 0.193$ ($p > 0.05$) was obtained, meaning there was no relationship between SHR and stroke. In the bivariate analysis in this study, no statistically significant relationship was found between SHR and stroke ($p = 0.193$). These results may indicate that although SHR can be used as a marker to predict certain cardiovascular events, there are limitations for cerebrovascular events such as stroke.

Table 4 SHR with rehospitalisation/revascularization

SHR	Rehospitalization/Revascularization				P value
	Yes		No		
	n	%	n	%	
<0.98	3	3%	36	36%	0,431
>0.98 s/d 1.32	5	5%	35	35%	
>1.32	4	4%	17	17%	

In table 4, related to the relationship between SHR and rehospitalization/revascularization, statistically using the chi square test or fischer exact test, a p value of 0.431 ($p > 0.05$) was obtained, meaning there was no relationship between SHR and rehospitalization/revascularization. This study also did not find a statistically significant relationship between SHR and rehospitalization or revascularization ($p = 0.431$). This may indicate that SHR is more closely related to acute hospitalization events than to long-term outcomes that depend on many other factors, such as the success of initial therapy, patient adherence to treatment, and progression of coronary disease.

Table 5 SHR with mortality

Table 3 SHR with mortality					
SHR	Mortality				P value
	Yes		No		
	n	%	n	%	
<0.98	11	11%	28	28%	0,721
>0.98 s/d 1.32	12	12%	28	28%	
>1.32	8	8%	13	13%	

In table 5, related to the relationship between SHR and mortality, statistically with the chi square test, the value of $p = 0.721$ ($p > 0.05$) means that there is no relationship between SHR and death. Like the relationship

between SHR and stroke and rehospitalization or revascularization, in this study there was no statistically significant relationship between SHR and death, with a value of $p = 0.721$. This result may indicate that SHR itself is not enough to be a predictor for the survival of ACS patients.

Table 6 SHR with MACE

SHR	MACE				P value
	Yes		No		
	n	%	n	%	
<0.98	15	15%	24	24%	0,001
>0.98 s/d 1.32	30	30%	10	10%	
>1.32	19	19%	2	2%	

In table 6, regarding the relationship between SHR and MACE, statistically using the chi square test, it was found that there was a relationship between SHR and MACE in ACS patients at HAM Hospital with a p value = <0.001 ($p < 0.05$). In this study, a statistically significant relationship was found between SHR and the incidence of MACE ($p < 0.001$). These results indicate the importance of SHR as a prognostic marker in ACS patients, especially in predicting cardiovascular events.

Table 7 SHR with MACE 3 points

SHR	MACE				P value
	Yes		No		
	n	%	n	%	
<0.98	2	5.1%	37	94.9%	0,477
>0.98 s/d 1.32	4	10%	36	90%	
>1.32	3	14.3%	18	85.7%	

In table 7, related to the relationship between SHR and MACE 3 points, statistically using the chi square test, there was no relationship between SHR and MACE 3 points in ACS patients at Adam Malik Hospital Medan with a value of $p = 0.477$ ($p > 0.05$). In this study, there was no relationship between SHR and MACE 3 points ($p = 0.477$).

4. Discussion

The demographic data in this study provide important context in understanding the relationship between SHR and MACE in ACS patients. The demographic characteristics obtained in this study, including age, gender, and measurements of patient glycemic control, can provide an overview of the patient population study. The average age of the study sample population was 59 years, with an age range of 39 to 81 years. This age distribution was found to be consistent with existing ACS epidemiological studies, which found that ACS incidence was higher in older age. As in the 2018 RISKESDAS, the prevalence of heart disease was found to be higher in the population aged over 55 years in Indonesia[11]. According to a study on ACS patients at the Dr. Soetomo Integrated Heart Service Center (Pusat Pelayanan Jantung Terpadu/PPJT) General Hospital, it was also found that 46% of the SKA research sample were aged 55-64 years[12]. The relatively larger age distribution in the elderly may also explain the high prevalence of MACE (64%) in this study, because as age increases, the risk factors for undesirable events and cardiovascular complications will increase[13].

The gender distribution in this study, with 78% male and 22% female, indicates a higher incidence of ACS in males. This result is not the same as the 2018 RISKESDAS survey which found that males compared to females were 1.3:1.6[15]. However, the results of this study are in accordance with the ACS study at RSU PPJT Dr. Soetomo, where 73% of ACS patients were male[12]. Glycemic control data in patients in this study included random blood sugar (GDS) and HbA1c. In this study, the average GDS was 190 mg/dL and the average HbA1c was 7.81%, indicating a lack of glycemic control in ACS patients in the study. Hyperglycemia is often found in patients with ACS and is associated with an increased risk of mortality. In a study by Babes et al (2022), it was found that 25–30% of hospitalized patients with ACS also had comorbid diabetes mellitus (DM)[14]. Montecucco et al (2023) found that the proportion of SKA patients with DM was very significant, with an increased risk of poor treatment outcomes. Blood glucose control is very important, even in the acute phase, to reduce complications[15].

In this study, a statistically significant relationship was found between SHR and heart failure in ACS patients with a p value = 0.000. This is in line with the findings of previous studies which stated that hyperglycemia triggered by stress can worsen myocardial dysfunction, contributing to the occurrence of heart failure.

Hyperglycemic stress was found to be closely related to cardiotoxic effects, in which SH and myocardium are directly related to cardiometabolic events involving inflammation, oxidative stress, and ischemia reperfusion [16]. A study by Modenesi et al (2012) found that 32.2% of ACS patients with hyperglycemic stress experienced progression to death and/or heart failure and/or left ventricular systolic dysfunction [17]. The stress hyperglycemia ratio (SHR) has attracted attention in recent years as a potential marker of cardiovascular stress. In the context of heart failure (HF), studies have shown that an elevated SHR during acute conditions may be indicative of poor outcomes. For example, hyperglycemia, as an adaptive response to physiological stress, exacerbates the inflammatory process, leading to worsening heart failure. A meta-analysis by Liu et al. (2020) concluded that a high SHR was associated with increased in-hospital mortality and adverse events in patients with acute heart failure, regardless of diabetes status. These findings reinforce the importance of SHR as a potential tool for risk stratification in heart failure patients, suggesting that even transient increases in glucose levels during periods of stress may be a predictor of cardiac dysfunction.

Although SH is a common manifestation found in stroke patients, the risk of stroke is influenced by many other factors, such as chronic atherosclerosis, atrial fibrillation, and blood pressure control, which may not be directly related to acute hyperglycemia conditions [18]. Although it is said that the presence of hyperglycemia is closely related to increased morbidity and mortality that can occur due to stroke, research that focuses on the relationship between SHR and stroke in ACS patients has not been found [19]. In stroke, stress hyperglycemia ratio (SHR) has been increasingly studied for its predictive value regarding patient outcomes. Acute hyperglycemia has been shown to worsen ischemic brain injury, leading to more severe stroke presentation and worse outcomes. A retrospective study by Jiang et al. (2024) showed that higher SHR in ischemic stroke patients was correlated with larger infarct size, increased rate of hemorrhagic transformation, and higher mortality, regardless of pre-existing diabetes. This suggests that stress hyperglycemia is not simply a reflection of a pre-existing metabolic condition, but a dynamic response that contributes to stroke severity [20].

In the event of ACS, rehospitalization is generally associated with many different cardiac conditions, including myocardial ischemia, atrial fibrillation and uncontrolled hypertension, and non-cardiac conditions such as lack of adherence to treatment, alcohol consumption, psychological and socioeconomic factors, and deficiencies in the health system [21]. A study by Bustea et al (2023) also showed that rehospitalization and revascularization in ACS patients were more associated with early ACS events that led to inpatient admission, such as STEMI, NSTEMI, UAP, and others [22]. Rehospitalization and need for revascularization are major concerns after cardiovascular events such as myocardial infarction or unstable angina. SHR has been evaluated in several studies to understand its role in predicting these outcomes. Lin et al. (2023) in their prospective cohort study found that patients with higher SHR were more likely to experience rehospitalization and post-discharge revascularization procedures, especially in non-diabetic individuals [23]. These findings suggest that SHR may be an independent risk factor for re-intervention in patients after percutaneous coronary intervention (PCI) or coronary vein bypass graft (CABG) surgery, indicating the need for tight glycemic control post-procedure.

In this study, it can be seen that the results of the analysis indicate that although SHR is related to the acute severity of the patient's condition, there are other variables that contribute to patient mortality. In previous studies, there was a relationship between hyperglycemia in the first 24 hours of hospitalization with 30-day and 180-day mortality of patients, but no study was conducted on deaths that occurred during the initial treatment period [24].

However, the results of the bivariate analysis in this study are not in line with the study by Xu et al (2022) which is a cohort study on the relationship between SHR and mortality in hospitalization in CHD patients. In the study by Xu et al (2022), a statistically significant relationship was found between SHR and the risk of death in hospitalization, with a p value <0.001. SHR was identified as an independent risk factor for mortality in hospitalization in CHD patients even after adjustment for other factors such as age, gender, BMI, blood pressure, smoking, alcohol consumption, eGFR, and others [25]. In research by Angeli et al (2010), a relationship was also found between new onset hyperglycemia and the risk of death during treatment, as well as 30-day and long-term mortality in ACS patients with a p value <0.0001 [26]. The relationship between stress-induced hyperglycemia and mortality has been the focus of several clinical studies, especially in critically ill patients. SHR, calculated as the ratio of admission glucose level to estimated mean glucose, has been identified as a powerful marker for predicting mortality, especially in acute medical conditions such as myocardial infarction, sepsis, and trauma. A study conducted by Wang et al. (2024) in patients hospitalized with acute coronary syndrome revealed that increased SHR significantly increased the risk of short-term and long-term mortality, regardless of diabetes status [27]. These data suggest that stress-induced hyperglycemia may be more than a by-product of acute illness, playing a contributory role in patient mortality through its association with systemic oxidative stress and inflammatory pathways.

In the study, the incidence of major cardiovascular events (MACE) observed was 64%, and showed that SHR can play an important role in risk stratification and help in determining high-risk patients for more intensive management. The results of this study are supported by research by Zeng et al (2023), which showed that SHR has a significant relationship to an increased risk of MACE events and indicates SHR as a marker that can be used for long-term risk stratification of ACS patients[28].

Yang et al (2022), who studied 5,562 patients with ACS undergoing PCI with MACC endpoints and a 2-year follow-up period showed a correlation between SHR and 2-year MACCE and MACE numbers showing a U-shape. The study stated that the use of SHR can be used for monitoring ACS patients, and assist in the preparation of management according to the patient's risk of MACE[29]. Abdu et al (2023) also found a 2,659-fold increase in the risk of ACS with SHR in data analysis using the Cox univariate regression model with a p value <0.001. Abdu et al stated that SHR correlates with markers of myocardial damage, such as cTnT, NT-proBNP and LVEF, which also indicates a contribution from SHR in showing an increased risk in ACS patients[30].

Acute hyperglycemia has a major effect on myocardial ischemia, and is known to promote apoptosis. Acute hyperglycemia is also known to decrease nitric oxide bioavailability, worsen endothelial function, increase platelet aggregation, and stimulate coagulation[31]. Based on this theory, it can also be concluded that the significant relationship between SHR and the incidence of MACE in ACS patients in this study occurred due to the patient's hyperglycemic stress conditions which worsened the prognosis. The use of SHR in stratifying the short-term and long-term risks of patients can also be used, which can later be used as a reference for planning the management of SKA patients. MACE, including myocardial infarction, stroke, and cardiovascular death, have been closely associated with stress hyperglycemia, especially in acute situations. SHR provides a more accurate picture of the state of transient hyperglycemia during acute stress than absolute glucose levels. A clinical study by Yang et al. (2022) has shown that patients with high SHR are at higher risk for MACE, regardless of whether they have pre-existing diabetes[10]. This association may be due to the effects of stress hyperglycemia on endothelial function, coagulation, and the inflammatory response, all of which may exacerbate atherosclerotic plaque instability, leading to events such as myocardial infarction or stroke.

In this study, SHR was found to be not significantly related to Major Adverse Cardiovascular Events (MACE) which include three main components, namely cardiovascular death, myocardial infarction, and stroke. These results are in line with several previous studies which stated that the relationship between SHR and MACE can vary depending on various clinical factors and patient characteristics[32].

Several studies have shown that SHR is more relevant for predicting short-term risk or certain types of cardiovascular events than for all types of MCA in the long term. In the study by Roberts et al. and Yang et al., very high or very low SHR values tend to be associated with the risk of adverse events in the acute phase, such as death during hospitalization or non-fatal myocardial infarction, especially in patients with acute coronary syndrome (ACS). This indicates that the acute glycemic response may better reflect the severity of the disease in the early phase, which may disappear over time or become less relevant in assessing the risk of long-term MCA[32,33].

One reason SHR may be less associated with MACE in the long term is variation in patient glycemic control and differences in disease characteristics. Patients with diabetes or prediabetes, for example, may have more complex glycemic patterns that are not always reflected in SHR as a single predictor. In addition, several studies have shown a non-linear U-shaped relationship between SHR and clinical events, where very low or high SHR values may be associated with poor clinical outcomes, whereas moderate SHR values may not significantly affect risk[32,33].

This study's strengths include its use of comprehensive medical records, minimizing bias, and its clinical relevance in highlighting the prognostic value of the Stress Hyperglycemia Ratio (SHR) in Acute Coronary Syndrome (ACS) patients. Robust statistical analysis further supports the findings. However, its retrospective design limits control over confounding factors, and the single-center setting at Adam Malik Hospital may reduce generalizability. The lack of prospective data and subgroup analyses, particularly for diabetic and non-diabetic patients, also limits interpretation. Future research should adopt a multicenter, prospective approach to validate SHR's role in predicting cardiovascular outcomes.

5. Conclusion and Future Research

Based on the results of the research and analysis conducted, the conclusions obtained are that out of the 100 study samples, the average age of the patients is 59 years \pm 10 years, with the majority being male. The study found a significant relationship between SHR and major cardiovascular events and was statistically significant but no relationship was found between SHR and MACE 3 Points.

For future researchers, it is recommended that further studies can be conducted on this research topic in prospective settings regarding the long-term impact of SHR on cardiovascular morbidity and mortality, especially in different patient subgroups, such as those with and without diabetes.

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Conflict of Interest

The authors declare no conflict of interest related to this study. The research was conducted independently, without any financial or personal relationships that could have influenced the results and interpretations presented in this manuscript.

References

- [1] 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 Neurol.* 2022 Sep 1;13:999536.
- [2] Xu W, Song Q, Wang X, Zhao Z, Meng X, Xia C, 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 Oct 19;21(1):217.
- [3] World Health Organization. 2021. Cardiovascular Disease (CVDs) [Updated 11 June 2021]. Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))
- [4] Badan Penelitian dan Pengembangan Kesehatan Republik Indonesia. 2018. Riset Kesehatan Dasar (RISKESDAS) 2018.
- [5] Perhimpunan Dokter Spesialis Jantung dan Pembuluh Darah Indonesia (PERKI). 2021. Pedoman Nasional Pelayanan Kedokteran Intervensi Koroner Perkutan
- [6] Poudel I, Tejpal C, Rashid H, Jahan N. Major Adverse Cardiovascular Events: An Inevitable Outcome of ST-elevation myocardial infarction? A Literature Review. *Cureus.* 2019 Jul 30;11(7):e5280
- [7] Liu HH, Cao YX, Jin JL, Guo YL, Zhu CG, Wu NQ, Gao Y, Zhang Y, Xu RX, Dong Q, Li JJ. Prognostic value of NT-proBNP in patients with chronic coronary syndrome and normal left ventricular systolic function according to glucose status: a prospective cohort study. *Cardiovasc Diabetol.* 2021 Apr 22;20(1):84
- [8] Roberts GW, Quinn SJ, Valentine N, Alhawassi T, O'Dea H, Stranks SN, et al. Relative hyperglycemia, a marker of critical illness: introducing the stress hyperglycemia ratio. *J Clin Endocrinol Metab.* 2015;100(12):4490–7.
- [9] Marenzi G, Cosentino N, Milazzo V, De Metrio M, Cecere M, Mosca S, et al. Prognostic value of the acute-to-chronic glycemic ratio at admission in acute myocardial infarction: a prospective study. *Diabetes Care.* 2018;41(4):847–53
- [10] Yang J, Zheng Y, Li C, Gao J, Meng X, Zhang K, et al. The impact of the stress hyperglycemia ratio on short-term and long-term poor prognosis in patients with acute coronary syndrome: insight
- [11] Kementrian Kesehatan Republik Indonesia. Hasil Utama Riset Kesehatan Dasar 2018. 2018. http://www.depkes.go.id/resources/download/utama/Hasil_Riset_Kesdas_2018
- [12] Qothi I, Fuadi MR, Subagjo A. Profile of Major Risk Factors in Acute Coronary Syndrome (ACS) at Pusat Pelayanan Jantung Terpadu (PPJT) Dr. Soetomo Public Hospital Surabaya between the Period of January–Desember 2019. *Cardiovascular Cardiometabolic Journal.* 2021;2:59-72.
- [13] Bosco, Elliott & Hsueh, Leon & McConeghy, Kevin & Gravenstein, Stefan & Saade, Elie. Major adverse cardiovascular event definitions used in observational analysis of administrative databases: a systematic review. *BMC Medical Research Methodology.* 2021. 21. 10.1186/s12874-021-01440-5.
- [14] Babes E.E., Bustea C., Behl T., Abdel-Daim M.M., Nechifor A.C., Stoicescu M., Brisc C.M., Moisi M., Gitea D., Iovanovici D.C., et al. Acute coronary syndromes in diabetic patients, outcome, revascularization, and antithrombotic therapy. *Biomed. Pharmacother.* 2022;148:112772. doi: 10.1016/j.biopha.2022.112772.
- [15] Stampouloulou, P. K., Anastasiou, A., Bletsas, E., Lygkoni, S., Chouzouri, F., Xenou, M., Katsarou, O., Theofilis, P., Zisimos, K., Tousoulis, D., Vavuranakis, M., Siasos, G., & Oikonomou, E. (2023). Diabetes Mellitus in Acute Coronary Syndrome. *Life (Basel, Switzerland)*, 13(11), 2226. <https://doi.org/10.3390/life13112226>

- [16] Scheen, M., Giraud, R., & Bendjelid, K. (2021). Stress hyperglycemia, cardiac glucotoxicity, and critically ill patient outcomes current clinical and pathophysiological evidence. *Physiological reports*, 9(2), e14713. <https://doi.org/10.14814/phy2.14713>
- [17] Modenesi, R.deF., Pena, F. M., Faria, C. A., Carvalho, R. V., Souza, N. R., Soares, J.daS., & Mesquita, E. T. (2012). Influence on prognosis and prevalence of stress hyperglycemia in a cohort of patients with acute coronary syndrome. *Revista Brasileira de terapia intensiva*, 24(4), 352–356. <https://doi.org/10.1590/s0103-507x2012000400010>
- [18] Capes, S. E., Hunt, D., Malmberg, K., Pathak, P., & Gerstein, H. C. (2001). Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke*, 32(10), 2426–2432. <https://doi.org/10.1161/hs1001.096194>
- [19] Angeli F, Reboldi G, Poltronieri C, et al. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. *Therapeutic Advances in Cardiovascular Disease*. 2015;9(6):412-424. doi:10.1177/1753944715594528
- [20] Jiang Z, Wang K, Duan H, Du H, Gao S, Chen J, Fang S. Association between stress hyperglycemia ratio and prognosis in acute ischemic stroke: a systematic review and meta-analysis. *BMC Neurol*. 2024 Jan 2;24(1):13.
- [21] Oliveira, L. M. S. M., Costa, I. M. N. B. C., Silva, D. G. D., Silva, J. R. S. S., Barreto-Filho, J. A. S., Almeida-Santos, M. A., Oliveira, J. L. M., Buarque, M. D. B. M., Vieira, D. A. D. S., & Sousa, A. C. S. (2019). Readmission of Patients with Acute Coronary Syndrome and Determinants. *Arquivos brasileiros de cardiologia*, 113(1), 42–49. <https://doi.org/10.5935/abc.20190104>
- [22] Bustea, C., Tit, D. M., Bungau, A. F., Bungau, S. G., Pantea, V. A., Babes, E. E., & Pantea-Roşan, L. R. (2023). Predictors of Readmission after the First Acute Coronary Syndrome and the Risk of Recurrent Cardiovascular Events-Seven Years of Patient Follow-Up. *Life (Basel, Switzerland)*, 13(4), 950. <https://doi.org/10.3390/life13040950>
- [23] Lin Z, Liang X, Zhang Y, Dai Y, Zeng L, Chen W, Kong S, He P, Duan C, Liu Y. Positive association between stress hyperglycemia ratio and pulmonary infection in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention. *Cardiovasc Diabetol*. 2023 Mar 31;22(1):76.
- [24] Deedwania, P., Kosiborod, M., Barrett, E., Ceriello, A., Isley, W., Mazzone, T., Raskin, P., & American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism (2008). Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation*, 117(12), 1610–1619. <https://doi.org/10.1161/CIRCULATIONAHA.107.188629>
- [25] Xu, W., Song, Q., Wang, X. 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* 21, 217 (2022). <https://doi.org/10.1186/s12933-022-01645-y>
- [26] Angeli, F., Verdecchia, P., Karthikeyan, G., Mazzotta, G., Del Pinto, M., Repaci, S., Gatteschi, C., Gentile, G., Cavallini, C., & Reboldi, G. (2010). New-onset hyperglycemia and acute coronary syndrome: a systematic overview and meta-analysis. *Current diabetes reviews*, 6(2), 102–110. <https://doi.org/10.2174/157339910790909413>
- [27] Wang WJ, Wang KX, Niu JL, Liu YX, Ge HL, Shen H; CCC-ACS investigators. Association between stress hyperglycemia ratio and in-hospital outcomes: findings from the improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome (CCC-ACS) Project. *J Geriatr Cardiol*. 2024 Jun 28;21(6):658-668. doi: 10.26599/1671-5411.2024.06.006. PMID: 38973822; PMCID: PMC11224654.
- [28] Zeng, G., Song, Y., Zhang, Z., Xu, J., Liu, Z., Tang, X., Wang, X., Chen, Y., Zhang, Y., Zhu, P., Guo, X., Jiang, L., Wang, Z., Liu, R., Wang, Q., Yao, Y., Feng, Y., Han, Y., & Yuan, J. (2023). Stress hyperglycemia ratio and long-term prognosis in patients with acute coronary syndrome: A multicenter, nationwide study. *Journal of diabetes*, 15(7), 557–568. <https://doi.org/10.1111/1753-0407.13400>
- [29] Yang, J., Zheng, Y., Li, C., Gao, J., Meng, X., Zhang, K., Wang, W., Shao, C., & Tang, Y.-D. (2022). 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*, 45(4), 947–956. <https://doi.org/10.2337/dc21-1526>
- [30] Abdu, F.A., Galip, J., Qi, P. et al. Association of stress hyperglycemia ratio and poor long-term prognosis in patients with myocardial infarction with non-obstructive coronary arteries. *Cardiovasc Diabetol* 22, 11 (2023). <https://doi.org/10.1186/s12933-023-01742-6>

- [31] Alavi-Moghaddam, M., Parsa-Mahjoob, M., Ghodssi-Ghassemabadi, R., & Bitazar, B. (2019). Association of Admission Blood Glucose Level with Major Adverse Cardiac Events in Acute Coronary Syndrome; a Cohort Study. *Archives of academic emergency medicine*, 7(1), e26.
- [32] Gian Paolo Fadini; Perturbation of Glucose Homeostasis During Acute Illness: Stress Hyperglycemia and Relative Hypoglycemia. *Diabetes Care* 1 April 2022; 45 (4): 769–771. <https://doi.org/10.2337/dci21-0069>
- [33] Ning Yan, Peng Wu, Zhengjun Zhang et al. Stress Hyperglycemia ratio in the prediction of 1-year outcomes in patients with acute myocardial infarction: A retrospective large sample cohort study, 16 August 2024, PREPRINT (Version 1) available at Research Square [<https://doi.org/10.21203/rs.3.rs-4744022/v1>]