International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 10, October 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.10.2024.104

Original Research

Analyzing the prognostic effects of admission hyperglycemia in individuals with acute myocardial infarction who are not diabetic

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Received Date: 17August, 2024 Accepted Date: 12 September, 2024

ABSTRACT

Aim: The aim of the present study was to assess the prognostic implications of admission hyperglycemia in non-diabetic acute myocardial infarction patients.

Methods: The present observationalenrolled consecutive NSTE-ACS patients treated at the Department of Cardiology for the period of 2 years. A total of 250 patients with NSTE-ACS and high BG without history of diabetes were enrolled.

Results: Age, sex, hypertension, hyperlipidaemia, smoking, and history of myocardial infarction ($p > 0:05$ for all) did not significantly differ among the three groups. The rates of multivessel disease, renal insufficiency, Killip grade III/IV, and emergency PCI, as well as the levels of high-sensitivity C-creatine kinase isoenzyme MB (CK-MB) ($p < 0:05$ for all), differed significantly across the three groups, however. Significantly more deaths, malignant arrhythmias, and severe pump failures occurred in groups B and C than in group A ($p < 0:05$). Group C had a greater incidence of malignant arrhythmia, severe pump failure, and mortality ($p < 0:05$) in comparison to group B.Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death.

Conclusion: In individuals with undiagnosed diabetes as opposed to those with established diabetes, hyperglycemia is a stronger predictor of adverse outcomes. Those who have never had diabetes treatment and are undiagnosed as diabetics may be more vulnerable, particularly if they have significant hyperglycemia.

Keywords: hyperglycemia, non-diabetic, acute myocardial infarction patients, prognosis

INTRODUCTION

Globally, acute coronary syndromes (ACS) constitute a major cause of mortality, with acute myocardial infarction (AMI) being particularly concerning due to its high short- and long-term death rates.[1] The World Health Organization (WHO) predicts that by 2030, there will be over 23.6 million cardiovascular deaths worldwide, marking a significant increase from previous decades.[2] Even in the absence of preexisting diabetes, hyperglycemia can emerge during an AMI due to stress-induced increases in catecholamines, steroids, and glucagon levels, along with a decrease in insulin levels.[3]

According to previous studies, 20 to 50% of patients with ST-segment elevation myocardial infarction (STEMI) experience stress hyperglycemia upon admission.[4,5] The American Heart Association and the Endocrine Society Clinical Guidelines define stress hyperglycemia as a random plasma glucose level above 140 mg/dL in both diabetic and non-diabetic hospitalized patients.[6] A study has highlighted that hyperglycemia, whether in diabetic or non-diabetic patients, adversely affects AMI outcomes.[7]

Research has shown that type 2 diabetes mellitus (T2DM) is a common comorbidity among patients with cardiovascular diseases, particularly AMI, and is detected in more than 20% of patients admitted for

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suspected AMI.[6] T2DM is associated with double the risk of in-hospital mortality and increases the likelihood of major adverse cardiovascular events (MACE) during follow-up.[6] Additionally, 10–20% of non-diabetic AMI patients exhibit significant hyperglycemia, which is linked to a higher risk of MACE.[7] Admission hyperglycemia is recognized as an independent predictor of poor short- and long-term outcomes in AMI patients.[8]

A study examining the prognostic significance of the stress hyperglycemia ratio (SHR) and admission blood glucose (ABG) levels in AMI patients found that elevated SHR and ABG levels are associated with increased 30-day and 1-year mortality, especially in diabetic patients.[9] For instance, Meshref[10] noted that hyperglycemia correlates with larger infarct sizes, greater summation of ST-segment elevation (sum STE), maximum ST-segment elevation (max STE), higher echocardiographic wall motion score index (WMSI), and a lower segmental ejection fraction (EF).Hyperglycemia generally increases the incidence of MACE, including re-hospitalization for heart failure, stroke, and coronary disease, in addition to raising mortality rates.[11] Regardless of whether thrombolysis or primary percutaneous coronary intervention (pPCI) is used as reperfusion therapy, hyperglycemia at admission is a significant predictor of adverse outcomes in AMI patients.[12,13]

The aim of the present study was to assess the prognostic implications of admission hyperglycemia in non-diabetic acute myocardial infarction patients.

MATERIALS AND METHODS

This was a retrospective analysis of prospectively enrolled consecutive NSTE-ACS patients treated at the Department of Cardiology for the period of 2 years. A total of 250 patients with NSTE-ACS and high BG without history of diabetes were enrolled.

NSTE-ACS was diagnosed on the basis of typical angina symptoms lasting for >10 minutes, accompanied by at least one of the following: ST-segment depression ≥ 0:5 mm, 0.5–1.0 mm transient ST-segment elevation in two consecutive leads for <30 minutes, T-wave inversion > 1 mm before the chest pain or within 12 hours after the chest pain, and/or myocardial enzymes (cardiac troponin T (TnT) or creatine kinase isozymes MB (CK- MB)) exceeding the upper limit of the normal values. Patients were excluded if they had past diabetes, incomplete clinical and coronary angiography data, admission BG level > 20 mmol/L, symptoms of ketoacidosis, and/or new-onset diabetes. A total of 250 patients with NSTE-ACS and high BG without history of diabetes were enrolled.

Research and Treatment Methods

Patients with suspected ACS underwent an electrocardiogram (ECG) and measurement of the BG level (hexokinase method, Olympus AU400) and myocardial injury markers. ACS was classified by the cardiovascular doctor into unstable angina pectoris, acute ST-segment elevation myocardial infarction, and acute NSTE myocardial infarction based on the ECG and levels of myocardial injury markers. Emergency coronary angiography was performed on patients in a critical condition, such as intractable or recurrent angina pectoris with dynamic ST-segment changes, heart failure, life-threatening arrhythmia, or hemodynamic instability. Stents were implanted in these patients according to the disease condition after the target vessel was determined. Other patients in a less critical state underwent percutaneous coronary intervention (PCI).

Based on the BG level, NSTE-ACS patients were divided into three groups: A (BG < 7:8 mmol/L), B (7:8 mmol/L ≤ BG < 11:1 mmol/L), and C (BG ≥ 11:1 mmol/L). The risk factors for ACS were recorded for each group, including age, hypertension, hyperlipidemia, smoking history, clinical biochemical indexes, inflammatory markers, and left ven-tricular ejection fraction as measured by echocardiography. SPSS software (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Differences were considered statistically significant at $p < 0:05$.

Data Quality Control

The quality of the statistical data affects the research accuracy. Data quality control requires scientific and rigorous work. In the context of big data, the quality and efficiency of hospital data should be continuously improved.

All of the departments providing the data were incorporated into the information construction by our hospital to establish an ideal data quality management system. The hospital employees continuously regularly their skills and were familiar with the operation process of the information sys- tem. Our hospital regularly monitored the data operation and randomly checked the quality and standardization of the statistical to identify and solve potential problems. This ensured smooth information interaction in the hospitaland improved the accuracy of the information. It also provided a solid foundation for the data quality control in our research.

Statistical Methods

SPSS software (version 25; IBM Corp., Armonk, NY, USA) was used to perform statistical analysis. Categorical variables are expressed as numbers or percentages. Means between the multiple groups were compared using one-way ANOVA.Multivariate logistic stepwise regression was used to calculate the odds ratio (OR) for the predictors of in-hospital death and their impact on the outcomes.

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RESULTS

Table 1: Comparison of the baseline characteristics of the three groups

Group(n)	*A(n=50)*	*B(n=100)*	*C(n=100)*	*p value*
Male,*n*	37	70	72	0.84
Age(year)	62±8	646	72±8	0.68
Hypertension,*n*	40	85	90	0.88
Hyperlipidemia,*n*	27	48	60	0.36
Smoking, *n*	30	64	72	0.76
Renal in adequacy,*n*	2	11	13	0.07
Oldmyocardialinfarction,*n*	5	18	22	0.28
Triple vessel disease,*n*	18	56	86	<0.01
Emergency PCI,*n*	33	75	80	0.02
Admission blood glucose(mmol/L)	6:2±3	9:3±1:5	17:5±4:4	<0.01
TnT,*n*	5	38	52	<0.05
CK-MB,*n*	2	24	45	<0.05
Killip gradingIII/IV,*n*	6	26	50	0.01
Hs-CRP(mg/L)	1:31±0:93	2:13±0:25	3:06±2:61	<0.01

There was no significant difference among the three groups in terms of age, sex, hypertension, hyperlipidemia, smoking, and history of myocardial infarction (p > 0:05 for all). However, there were significant differences among the three groups in the incidences of the multivessel disease, renal insufficiency, Killip grade III/IV, and emergency PCI (p < 0:05 for all), as well as the levels of high-sensitivity C-creatine kinase isoenzyme MB (CK-MB) (p < 0:05 for all).

Table 2: Comparison of in-hospital outcomes of the three groups

Groups	Number	Pump failure, *n*(%)	Malignant arrhythmia, *n*(%)	Target lesion revascularization, *n* (%)	Death, *n*(%)
A	50	6(12)	4 (8)	2(4)	2(1)
B	100	26(26)	11(11)	4(4)	6(6)
C	100	36(36)	25(25)	6(6)	12(12)

The incidences of severe pump failure, malignant arrhythmia, and death were significantly higher in groups B and C than in group A (p < 0:05). The incidences of severe pump failure, malignant arrhythmia, and death were higher in group C than in group B (p < 0:05).

Table 3: Multivariate logistic regression analysis of in-hospital death

Item	Odds ratio	95%CI	*P* value
Age	1.05	(0.91,1.14)	0.25
Hyperglycemia at admission	1.84	(1.26,2.41)	<0.01
Killip gradingIII/IV	2.16	(1.03,3.96)	0.03
Renal insufficiency	1.16	(1.03,1.21)	0.07

Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death.

DISCUSSION

Diabetes is an important independent risk factor for coronary atherosclerosis. Many previous studies have confirmed that hyperglycemia at admission is common in patients with acute coronary syndrome (ACS), and it is a risk factor for inhospital death and complications.[14-17] Previous epidemiological studies showed that 25–50% of ACS patients had elevated blood glucose (BG) level at admission. Recent studies suggest that the effects of hyperglycemia on the prognosis of ACS differ between diagnosed and undiagnosed diabetes. Hyperglycemia is a stronger predictor of adverse events in ACS patients without known diabetes than those with history of diabetes.[18,19]

There was no significant difference among the three groups in terms of age, sex, hypertension, hyperlipidemia, smoking, and history of myocardial infarction (p > 0:05 for all). However, there were significant differences among the three groups in the incidences of the multivessel disease, renal insufficiency, Killip grade III/IV, and emergency PCI (p < 0:05 for all), as well as the levels of high-sensitivity C-creatine kinase isoenzyme MB (CK-MB) (p < 0:05

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for all).Studies have found that admission hyperglycemia was the greatest risk factor for patients with acute myocardial infarction without diabetes. The 30-day mortality rate of patients without diabetes increased when the admission BG level exceeded 6.1 mmol/L, while the admission BG threshold for the 30-day mortality rate was higher in diabetic patients. Additionally, the increased risk of death associated with high BG level was not limited to known diabetic patients; rather, the mortality rate of patients without diabetes was higher than that of diabetic patients.[20,21] Yacov et al[22] reported that admission hyperglycemia was an independent risk factor for acute kidney injury in nondiabetic ST-segment elevation myocardial infarction patients undergoing primary PCI.

The incidences of severe pump failure, malignant arrhythmia, and death were significantly higher in groups B and C than in group A ($p < 0:05$). The incidences of severe pump failure, malignant arrhythmia, and death were higher in group C than in group B ($p < 0:05$). Ozge et al[23] reported that elevated admission BG level attenuated the coronary collateral flow in patients with ST-elevation myocardial infarction. Satoshi et al[24] pointed out that glycemic variability was associated with myocardial damage after PCI in nondiabetic ST-segment elevation myocardial infarction patients. Microvascular dysfunction has also been confirmed in acute myocardial infarction patients with hyperglycemia in the study of Simsek et al[25] that evaluated the association of acute-to-chronic glycemic ratio and no reflow in patients with ST-segment elevation myocardial infarction undergoing primary PCI. Shock index on admission was associated with coronary slow/no reflow in patients with acute myocardial infarction undergoing emergent PCI. Wang et al[26] found a higher incidence of no blood flow in patients with hyperglycemia after successful reperfusion.

The relationship between glycemic level on-admission and short term prognosis has been thoroughly investigated in previous studies, however the mechanisms underlying the association between high serum glucose levels and mortality are not fully understood. It is indeed not clear if hyperglycemia isdirectly implicated in cellular damage or just an associatedepiphenomenon and a marker of high stress levels and adrenergic response.[27,28]Logistic regression analysis was performed with in-hospital death as the dependent variable and the previously identified risk factors as independent variables. The results showed that hyperglycemia, age, renal insufficiency, and severe pump failure were risk factors of in-hospital death.Inacutely hyperglycemic mice, the level of tissue plasminogen activator was decreased and the level of plasminogen activation inhibitor was increased. Hyperglycemia in type 2 diabetic patients (abnormal glycemic clamp technique) was associated with increased activity of thromboxane A2 (TXA2) and von Willebrand factor. Acute hyperglycemia caused fibrinogen t1/2 to decrease and induced platelet aggregation, thereby increasing the levels of fibrinogen A, prothrombin, and factor VII levels. These changes indicate a prothrombotic state. The increased BG level was accompanied by increased vascular inflammatory markers.[29,30]

CONCLUSION

Therefore, hyperglycemia has different effects on the prognosis of patients with diabetes or undiagnosed diabetes. Hyperglycemia is more predictive of adverse events in patients with undiagnosed diabetes compared to those withdiagnosed diabetes. Although the pathophysiological mechanism underlying this phenomenon is unknown, there are several explanations. Some undiagnosed diabetic patients, especially those with severe hyperglycemia, may be at high risk because they have never been treated for diabetes. In addition, in patients with unknown diabetes and hyperglycemia, when acute myocardial infarction occurs, even if blood glucose was significantly elevated, insulin therapy was rarely used.In view of the possible beneficial effect of insulin on myocardial ischemia, this difference in treatment may explain the different prognosis. Finally, it is possible that similar BG level may represent a more serious condition in unknown diabetic patients. There are still many gaps in understanding the relationship between hyperglycemia and the adverse prognosis. Further studies are needed to confirm whether hyperglycemia is an indicator of high mortality.

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