

## Research Article

# Relation between Stress Hyperglycemia and Mortality in Patients with Acute Myocardial Infarction

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### Abstract

**Objectives:** Acute myocardial infarction (AMI) is one of the leading causes of death in industrialized countries. Hyperglycemia and impaired glucose tolerance are common during AMI. We aimed to investigate the effect of stress (acute) hyperglycemia on mortality in patients with AMI who were not previously diagnosed with diabetes mellitus (DM).

**Methods:** We retrospectively reviewed 307 patients with acute coronary syndrome (ACS) who were admitted to the Emergency Department of Batman Regional State Hospital between January 1, 2014 and January 1, 2018. Stress hyperglycemia was considered to be present in patients with no DM history with a blood glucose level of >140 mg/dL or who had an HbA1c value of <6.5 in the last 3 months.

**Results:** Of the 307 patients in our study, 211 (68%) were male and 96 (32%) were female. Stress hyperglycemia was detected in 141 (45.9%) of the patients. It was found that 69% of patients with stress-related hyperglycemia had ST segment elevation myocardial infarction (STEMI) and 31% had non-ST segment elevation myocardial infarction (NSTEMI). We found that the rate of STEMI detection in patients with stress hyperglycemia was statistically significantly higher than that in NSTEMI ( $p<0.001$ ). We found a significant relationship between the duration of hospital stay and hyperglycemia compared with the duration of hospitalization with stress hyperglycemia ( $p=0.01$ ). In total, 24 patients (7.8%) died. Stress hyperglycemia was present in 66.1% of patients with exclusion, whereas 33.9% of patients did not have stress hyperglycemia. We found a statistically significant relationship between exclusion patients and stress hyperglycemia ( $p=0.002$ ).

**Conclusion:** We found a significant association between stress hyperglycemia and mortality and duration of hospital stay in patients with AMI. We believe that prognosis and mortality of patients with AMI can be predicted using blood sugar level at the time of admission.

**Keywords:** Acute myocardial infarction, mortality, stress hyperglycemia

Ischemic necrosis of the myocardium is called myocardial infarction. Despite improvements in medical and interventional therapies in recent years, acute myocardial infarction (AMI) is still an important cause of mortality and morbidity. In a study conducted in our country, it was reported that approximately 230.000 new coronary events occurred annually and coronary death occurred in approximately 66.000 men and 61.000 women.<sup>[1, 2]</sup> AMI usually occurs when the blood flow in a coronary artery is

obstructed by atherosclerosis or is suddenly interrupted.<sup>[3]</sup> The American Diabetes Association (ADA) 2009 guidelines describe stress hyperglycemia as having plasma glucose levels of 140 mg/dL at any given time in hospital patients.<sup>[5]</sup> Stress hyperglycemia describes an impaired metabolic state that has not been previously diagnosed with diabetes mellitus (DM), but is temporarily elevated in plasma blood sugar levels during an acute illness.<sup>[6]</sup> Hyperglycemia and impaired glucose tolerance are common during AMI. Hy-

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perglycemia seen at the onset of AMI appears to be associated with the introduction of stress mechanism, which is a reflection of high free fatty acids, insulin resistance, and steroid hormones.<sup>[7]</sup> In fact, this mechanism, which enters the circuit to adapt to the stress situation, becomes harmful to the mitochondrial damage, oxidative stress-related damage in the cells, and affects the course of the disease in the worst way.<sup>[2, 8, 9]</sup> We aimed to investigate the effects of stress (acute) hyperglycemia on mortality in patients with acute coronary syndromes (ACS) who did not previously diagnosed with DM.

## Methods

In this study, 307 patients admitted to the Emergency Department of Batman Regional State Hospital between January 1, 2014 and January 1, 2018 and diagnosed with ACS were retrospectively studied. Considering the American Diabetes Association's (ADA) 2009 guidelines for stress-induced hyperglycemia, stress hyperglycemia was considered to be present in patients with no DM history with a blood glucose level of >140 mg/dL or who had an HbA1c value of <6.5 in the last 3 months. A local committee approved the study. Patients were included in the study if they had (at least two findings) chest pain, electrocardiography (ECG) findings, and elevated CK-MB/troponin values at the time of admission or if they underwent angiography and did not have a history of DM. Patients with DM, comorbid diseases, septicemia, and endocrine disorders, those who used medications that affected blood glucose levels (beta blockers, thiazides, glucocorticoids), those with HbA1c values > 6.5%, and cases that were not accessible from file and automation systems were excluded.

## Statistical Analysis

Univariate statistical analyses were performed using chi-square test for categorical variables and Student's t test for continuous variables. Numerical variables were considered as mean±SD. P<0.05 was considered statistically significant.

**Table 1.** Distribution of ECG findings

	Number (n)	%
Sinus rhythm	76	24.7
Inferior MI	82	27.8
Anterior MI	71	23.1
Posterior MI	17	5.5
Anterior+inferior MI	14	4.5
Anterior+lateral MI	12	3.9
Inferior+posterior MI	24	7.8
Asystole	11	3.5
Total	307	100

## Results

We included 307 patients who met the criteria; 211 (68%) were male and 96 (32%) were female. The mean age of the patients was calculated as 52.61±15.93 years.

When the ECG findings of patients admitted to the hospital were examined, it was determined that 76 (24.7%) patients had normal sinus rhythm in the first ECG findings. ECG of ST segment elevation myocardial infarction (STEMI) patients was the most common inferior wall infarction (n=82%, 27.8%) (Table 1).

Of all the patients, 191 (66%) were diagnosed with non-ST segment elevation myocardial infarction (NSTEMI) and 105 (34%) were diagnosed with STEMI. When male and female sexes were compared, there was no significant difference between the groups in terms of STEMI and NSTEMI distribution (p>0.05).

Of all the patients, 98.5% had coronary angiography, and the most common (84.9%) left anterior descending (LAD) artery stenosis was detected.

Stress hyperglycemia was detected in 141 (45.9%) patients. It was determined that 30.1% of patients with stress hyperglycemia and 29.3% of patients without stress hyperglycemia were female. There was no statistically significant difference between the presence of stress hyperglycemia and sex (p>0.05).

There was no statistically significant difference between the groups in terms of ECG findings when compared with patients with stress hyperglycemia (p>0.05).

STEMI was found in 69% of patients with stress hyperglycemia, STEMI in 31%, STEMI in 52.5%, and NSTEMI in 47.5% of patients without stress hyperglycemia. We found that the rate of STEMI detection in patients with stress-related hyperglycemia was statistically significantly higher than that of NSTEMI (p<0.001) (Table 2).

Stress hyperglycemia was detected in 69.1% of patients who underwent stenosis in LAD and in 61.3% of patients who underwent stenosis in the right coronary artery (RCA). We found a statistically significant relationship between stress hyperglycemia and RCA and LAD stenosis (Table 3).

The mean duration of hospitalization was 6.07±4.3 days. We found a significant relationship between the duration of hospital stay and hyperglycemia when compared with

**Table 2.** Relationship between stress hyperglycemia and MI types

	STEMI (%)	NSTEMI (%)	p
Stress hyperglycemia	n=97 (69)	n=44 (31)	<0.001
No stress hyperglycemia	n=87 (52.5)	n=79 (47.5)	0.49

**Table 3.** Relationship between stress hyperglycemia and coronary angiography findings

	Stress hyperglycemia %	No stress hyperglycemia %	p
Stenosis in LAD	69.1	30.9	<0.001
Stenosis in LCMA	54.6	45.4	0.53
Stenosis in Cxa	48.2	51.8	0.47
Stenosis in RCA	61.3	38.7	<0.001

LCMA: Left coronary main artery; LAD: left anterior descending artery; Cxa: circumflex artery; RCA: Right coronary artery.

the duration of stress inpatients with stress hyperglycemia ( $p=0.01$ )

In total, 24 patients (7.8%) died. Stress hyperglycemia was present in 66.1% of patients with exclusion, whereas 33.9% of patients had no stress hyperglycemia. We found a statistically significant relationship between exclusion patients and stress hyperglycemia ( $p=0.002$ ).

## Discussion

Coronary artery disease is the leading cause of mortality and morbidity in the developed countries.<sup>[10]</sup> Turkey has been among the causes of death.<sup>[1, 11]</sup> Many studies have emphasized that patients with stress-related hyperglycemia have an adverse effect on the mortality and duration of hospitalization of patients with acute cardiovascular disease.<sup>[2, 7, 12, 13]</sup> Stress hyperglycemia in the onset of AMI appears to be due to the stress mechanism and is a reflection of the increased levels of adrenaline, glucagon, and steroid hormones, together with increased free fatty acids.

Apart from necrotic dead tissue in the area of the infarct, AMI has a field of apoptotic dead cells in the peri-infarct area.<sup>[14]</sup> Free oxygen radicals formed by hyperglycemia have been shown to induce apoptosis in cardiomyocytes by triggering the cytochrome-C and KASPAS-3 pathway.<sup>[15]</sup> Insulin stimulates nitric oxide (NO) synthesis. Increased blood flow through NO-induced vasodilatation accelerates glucose uptake into tissues. In the case of insulin resistance, insulin is reduced by vasculoprotective effects via NO. Atherogenic effects via vascular smooth muscle cell proliferation, migration, and production of plasminogen activator inhibitor (PAI-1) are accelerating.<sup>[16]</sup> Clinical trials have shown that insulin resistance may also be important in the expression and regulation of PAI-1, an independent risk factor for coronary artery disease.<sup>[17]</sup> Due to the increase in PAI-1 levels, impaired fibrinolytic activity and susceptibility to coagulation are expected in hyperinsulinemia.<sup>[18]</sup>

There are studies linking post-AMI hyperglycemia with increased cardiac insufficiency, cardiogenic shock, arrhythmia,

and hospital mortality independent of diabetes status.<sup>[19]</sup> Again, studies have shown that hyperglycemia increases the risk of mortality during cardiopulmonary bypass.<sup>[20]</sup>

We found a significant association between stress hyperglycemia and mortality and duration of hospital stay in patients with AMI in our study. We believe that prognosis and mortality can be predicted in patients with AMI using the blood sugar level at the time of admission. We consider that prospective, multicentre studies on this subject will contribute to the literature.

## Conclusion

In conclusion, the prolongation of mortality and hospital stay in patients with AMI and hyperglycemia highlights the importance of checking the glucose levels as early as possible in these patients to prevent future adverse cardiovascular events. This will also give us the ability to predict the prognosis of patients.

## Disclosures

**Ethics Committee Approval:** The study was approved by the Local Ethics Committee.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship contributions:** Concept – N.G.K., M.O., M.U.; Design – N.G.K., M.O., M.U.; Supervision – N.G.K., M.O., M.U.; Materials – N.G.K., M.O., M.U.; Data collection &/or processing – N.G.K., M.O., M.U.; Analysis and/or interpretation – N.G.K., M.O., M.U.; Literature search – N.G.K., M.O., M.U.; Writing – N.G.K., M.O., M.U.; Critical review – N.G.K., M.O., M.U.

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