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The new biomarker that predicts in-hospital mortality in myocardial infarction: glucose/potassium ratio

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ABSTRACT

Aims: Acute myocardial infarction (AMI) remains one of the leading causes of cardiovascular mortality. However, the parameters used to predict short-term mortality are limited. Glucose-potassium ratio (GPR) is a new biomarker that has been recently used. This study aimed to investigate the usefulness of GPR in predicting short-term mortality in patients diagnosed with AMI in the emergency department.

Methods: This retrospective cohort study was conducted between January 1, 2022, and June 30, 2022, and included patients registered in the hospital emergency health system with IRB (Institutional Review Board) approval. Patients were identified based on inclusion criteria, and their demographic data, laboratory findings, and outcomes were recorded in the hospital registration system. Data comparisons between deceased and non-deceased patients were performed using the Student's t-test. Correlation analysis was performed using Spearman's correlation coefficients. A binary logistic regression model was created to determine the predictive parameters, and odds ratios and 95% confidence intervals (CI) were presented.

Results: A total of 665 patients diagnosed with AMI were included in the study, with 75.9% of all patients being male and an average age of 62.14±11.62. A total of 6.6% of the patients included in the study died due to various causes during hospitalization. When laboratory values of deceased AMI patients were examined, statistically significant increases in glucose, urea, creatinine, WBC, neutrophil, lymphocyte, troponin, ckmb, and lactate levels were observed. The effects of GPR, Neutrophil-to-lymphocyte ratio (NLR) , Platelet to Lymphocyte ratio (PLR), lactate, and troponin levels on in-hospital mortality were analyzed using univariate logistic regression. GPR (95% CI 1.015-1.036, p=0.000), troponin (95% CI 1.001-1.001, p=0.000), and lactate (95% CI 1.437-1.908, p=0.000) were found to be the most important factors associated with mortality in patients with AMI. The ability to predict in-hospital mortality in AMI was compared, and GPR was found to have a higher predictive ability than troponin, a biomarker of myocardial damage (area under the curve (AUC): 0.729; p=0.000; Sensitivity: 70%; Specificity: 70%; Cut-off: 38.21).

Conclusion: GPR, as a new and inexpensive biomarker, can be used to determine in-hospital mortality in patients with AMI. This index has a better predictive ability than troponin, NLR, and PLR, but is weaker than lactate.

Keywords: Acute myocardial infarction, glucose-potassium ratio, short-term mortality

INTRODUCTION

Acute myocardial infarction (MI) ranks among the top three causes of cardiovascular deaths along with acute pulmonary embolism and stroke, and its mortality rate remains quite high. Approximately 5.5% to 18.2% of patients who experience myocardial infarction die in the hospital, while long-term follow-up shows that this mortality rate can reach up to 15%.[1-4]

Studies have shown that inflammation plays a significant role in the development of cardiovascular disease and atherosclerosis.[5,6] Therefore, inflammation and oxidative stress may cause plaque rupture that leads to cardiovascular events.[7,8] In particular, an inflammatory and neuroendocrine response occurs after acute stress. This response leads to an increase in the release of counter-regulatory hormones as a result of the activation of the hypothalamic-pituitary-adrenal system by stressor factors. The release of these hormones affects glucose and potassium metabolism.[9] In response to stress hormones, the release of inflammatory mediators and procoagulation factors increases, and as a result, glucose utilization decreases in peripheral tissues. Hyperglycemia further increases due to the release of counter-regulatory hormones. This event creates a vicious cycle that increases proinflammatory and procoagulation cytokine secretion, inflammatory response, and oxidative stress.[10] A study showed that the glucose-potassium ratio (GPR) could be a good indicator of vasospasm and stress response in patients with subarachnoid hemorrhage.[11] Hyperglycemia is frequently observed in patients who present with acute myocardial infarction (AMI), regardless of whether they have a previously documented diabetes mellitus (DM).[12] Particularly, significant hyperglycemia is present in approximately 10% to 20% of non-diabetic AMI patients.[13]

As a result of the increased release of counter-regulatory hormones secondary to this hyperglycemia, a decrease in extracellular potassium level will occur. Taking all these physiological responses into account, we believe that the evaluation of glucose and potassium values together can be very useful in understanding the endocrine and metabolic effects on the disease and its consequences. This study aimed to investigate whether GPR has the potential to predict prognosis and whether it would be useful in predicting the risk of in-hospital mortality when used routinely.

METHODS

Study Design and Participants

The study was designed as a retrospective cross-sectional clinical cohort. All patients diagnosed with myocardial infarction in the emergency department and undergoing emergency coronary angiography by the cardiology department between January 1, 2022, and June 30, 2022, were included in the study. Patients' demographic data (age, gender) were investigated through the hospital registration system. Standard treatment protocols were applied to all patients in the emergency department. This study was conducted with the approval of our institution's Ethics Committee (Date: 05.01.2023, Decision No: 01-21). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients under the age of 18, patients whose demographic characteristics and medical history could not be obtained from the hospital registration system, patients whose parameters at the first laboratory values in the emergency department could not be obtained, patients whose outcome status could not be reached, pregnant patients, and patients who did not undergo emergency angiography were excluded from the study. After applying inclusion and exclusion criteria, 158 patients were excluded and 665 patients were included in the study (**Figure 1**).

For all patients who were diagnosed with AMI before coronary angiography, blood samples were taken from the antecubital vein with atraumatic insertion and immediately sent to the laboratory. Peripheral venous blood samples were taken from all patients for glucose, sodium, potassium, urea, creatinine, CK-MB, cardiac troponin, lactate, white blood cells (WBC), neutrophils, lymphocytes, platelets, and other routine laboratory parameters at the time of admission. An EDTA (ethylenediaminetetraacetic acid)-containing blood tube was used for hematological evaluation. The complete blood count, including differentials, was calculated using an automated blood cell counter (Sysmex xn1000 series, USA). The biochemical panel was measured with a Cobas 6000 (Roche Diagnostics, USA) autoanalyzer. GPR was obtained by dividing glucose levels by potassium levels using the MS Excel program.

Statistical Analysis

In this study, a p value of <0.05 was considered statistically significant. Therefore, statistical analysis was performed using IBM Company's SPSS Statistics for Windows program version 20. The normality of distribution was evaluated using the Kolmogorov-Smirnov test, and since continuous variables were normally distributed, all results were presented as mean±standard deviation. All categorical variables were analyzed using chi-square test and presented as frequency (%). Data comparisons between non-fatal AMI and fatal AMI were performed using the Student's t-test. Correlation analysis was performed using Spearman correlation coefficients. To determine predictive parameters, we constructed a binary logistic regression model containing significant variables according to univariate evaluation, and presented odds ratios and 95% confidence intervals (CI) (**Table 1**). Receiver operating characteristic (ROC) curve analysis was performed to evaluate the prognostic accuracy of GPR for fatal AMI compared to non-fatal AMI, and the area under the curve (AUC) was estimated.

RESULTS

Demographic and Clinical Findings

During the study period, 823 patients who were diagnosed with myocardial infarction and underwent coronary angiography in the emergency department were identified. Subsequently, 158 patients were excluded due to the specified reasons (**Figure 1**).

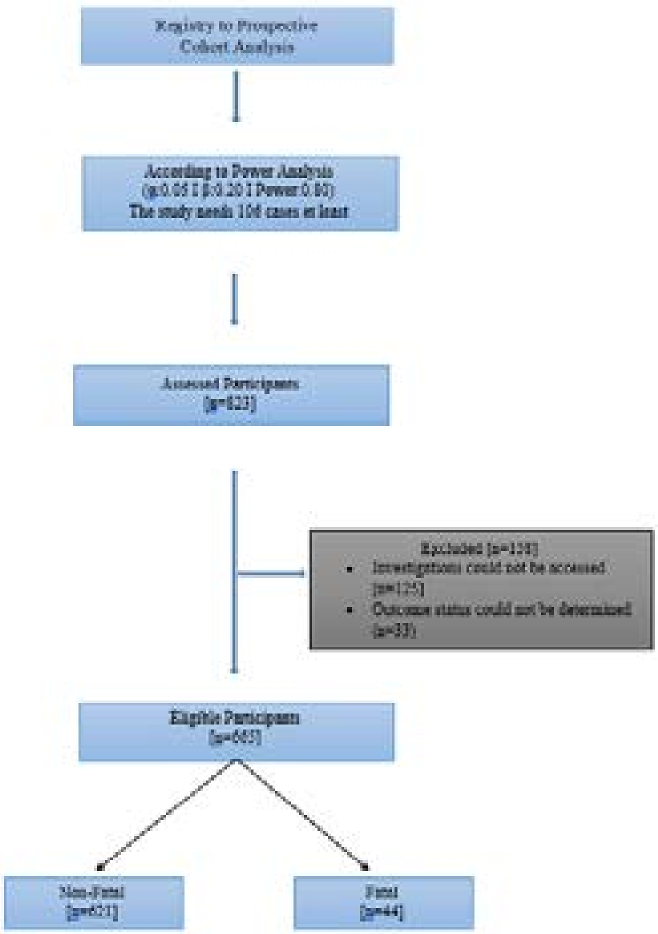

Figure 1. The flow chart for the selection and enrollment of study participants

665 patients were recorded for analysis. During hospitalization, 44 of the included patients died due to various reasons. Among all patients, 75.9% were male and 24.1% were female, with a mean age of 62.14±11.62. The demographic characteristics and laboratory values of the patients are presented in **Table 1**.

Table 1. Main characteristics of patients

Variables	Acute myocardial infarction (AMI)		
	Non-fatal AMI	Fatal AMI	P value
Gender (M/F)	475/30	146/14	.213
Age,year	61.70±11.84	68.27±11.62	**.000**
Glucose, mg/dl	164.47±96.73	266.52±162.98	**.000**
Sodium, mmol/L	138.91±2.76	137.65±3.70	**.005**
Potassium, mmol/L	4.47±0.51	4.66±0.76	**.031**
Urea, mg/dl	17.50±8.07	23.88±10.25	**.000**
Creatinine, mg/dl	0.98±0.39	1.25±0.39	**.000**
WBC, 10^3 /µL	10.95±3.73	17.04±8.28	**.000**
Platelet, 10^3 /µL	254.75±75.04	238.38±91.12	**.020**
Neutrophil, 10^3 /µL	7.86±3,58	12.52±6.83	**.000**
Lymphocyte, 10^3 /µL	2.26±1.24	3.45±3.13	**.000**
Troponin, ng/L	311.78±585,38	1534.68±2217.41	**.000**
CK-MB, µg/L	23.70±40.57	61.22±84.89	**.000**
Lactate, mmol/L	2.35±1.27	5.36±4.23	**.000**
NLR	4.83±4.41	6.41±4.59	**.022**
PLR	145.15±104.13	149.13±113.73	.808
GPR	36.82±19.93	57.60±34.23	**.000**

WBC: White blood cell, CK-MB: Creatine kinase-myocardial band, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, GPR: Glucose to potassium ratio. Bold values means the significance of p<0.005. "Gender" parameter was analyzed by the Chi-Square test, while the others (mean±standart deviation) were done using the independent Student T-test

When comparing fatal and non-fatal AMI, no significant difference was observed between the two groups in terms of gender. However, when other parameters were compared between the two groups, it was found that glucose, potassium, urea, creatinine, WBC, neutrophil, lymphocyte, troponin, ckmb, and lactate values significantly increased in fatal AMI patients, while sodium and platelet values decreased.

In this study, we analyzed the effect of glucose-to-potassium ratio, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lactate ratio, and troponin ratio on in-hospital mortality in AMI patients using univariate logistic regression (**Table 2**). The results indicated that GPR (95% CI 1.015-1.036, p=0.000), troponin (95% CI 1.001-1.001, p=0.000), and lactate (95% CI 1.437-1.908, p=0.000) were the most significant factors associated with mortality in patients with AMI.

Table 2. Logistic regression analysis for in-hospital mortality in AMI

Variables	Odds ratio (95% confidence interval)	P value
Troponin, ng/L	1.001 (1.001-1.001)	.000
Lactate, mmol/L	1.656 (1.437-1.908)	.000
NLR	0.999(0.992-1.006)	.823
PLR	1.000 (0.998-1.003)	.776
GPR***	1.026 (1.015-1.036)	.000

GPR: Glucose to Potassium ratio, NLR: Neutrophil to Lymphocyte ratio, PLR: Platelet to Lymphocyte ratio, AMI: Area under the curve.
*Results are presented as odds ratios (95% confidence interval).

Furthermore, we compared the ability of these indicators to predict in-hospital mortality in AMI patients. GPR showed a high predictive ability for in-hospital mortality in AMI patients, which was similar to troponin, a biomarker of myocardial damage. When compared to NLR and PLR, which have been suggested as indicators of in-hospital mortality in recent studies and have a direct effect on thrombus formation, GPR was found to have a higher predictive ability for mortality (**Table 3** and **Figure 2**). Therefore, we believe that GPR is an important predictor of in-hospital mortality in AMI patients and requires further investigation.

Table 3. Comparison of the effects of group S and group R+S on SBT, SET, MAS9, and seizure durations

Variables	Area	SE[a]	Sig[b]	95% Cl		SN (%)	SP (%)	Cut-off
				Lower	Upper			
Troponin, ng/L	0.726	0.042	0.000	0.643	0.808	65	63	171.3
Lactate, mmol/L	0.782	0.037	0.000	0.709	0.855	77	69	2.55
NLR	0.591	0.053	0.044	0.488	0.694	59	59	4.17
PLR	0.465	0.057	0.435	0.353	0.577	45	45	111.56
GPR	0.729	0.041	0.000	0.649	0.808	70	70	38.21

NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, GPR: Glucose to potassium ratio, SE: Standart error, SN: Sensitivity, SP: Specificity.
[a] Under the nonparametric assumption.
[b] Null hypothesis: true area=0.5.

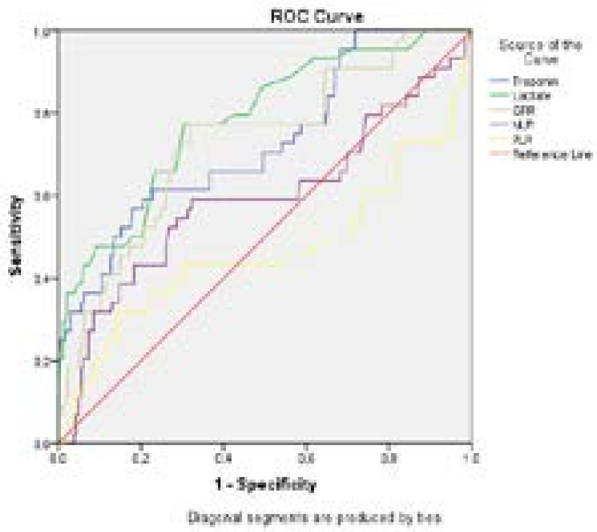

Figure 2. ROC Curve showing the diagnostic effectiveness of Troponin, lactate, NLR, PLR, and GPR for AMI

DISCUSSION

Upon reviewing the literature, this study is the first to investigate the role of GPR in AMI. We found that GPR, a new ratio, is at least as useful as troponin in assessing in-hospital mortality in patients diagnosed with AMI, but weaker than lactate. Additionally, we found that GPR has a superior predictive rate compared to other blood parameters that play an effective role in thrombus formation. We believe that GPR can be used as a diagnostic index to predict in-hospital mortality in patients diagnosed with AMI and can open up new horizons in this field.

Many studies have shown that hyperglycemia in the context of AMI is an independent determinant of heart failure and mortality, regardless of diabetic status.[14-17] Keiichi et al.[18] investigated the effect of glycemic variability on myocardial infarction size in patients with ST-segment elevation myocardial infarction and showed that patients with high glycemic variability had larger infarct sizes than expected. In addition, in studies on the control of hyperglycemia in intensive care unit follow-up of patients with acute coronary syndrome, it has been shown that keeping the glucose level between 1.26 g/L and 1.80 g/L reduces 3-month, 1-year, and 3-year mortality. Moreover, the results of this study were independent of the insulin protocol used.[19] All of these findings support the notion that controlling stress hyperglycemia to a certain degree can reduce mortality and morbidity rates.

Potassium levels, which are abundant in cells, are regulated by the Na/K ATP pump located on the cell surface. Increasing adrenergic hormones in stress up-regulate this pump, resulting in a decrease in K+ levels.[20,21] The hyperglycemic state that occurs due to increased catecholamine discharge in AMI results in increased insulin secretion and intracellular K+ uptake. The serum GPR index is a very new parameter analyzed in circulation diseases such as stroke and hemorrhage. Matano et al.[22] reported that GPR has a strong relationship with vasospasm occurring in cerebral infarctions. Wu et al.[23] reported in a recent study that increased serum GPR in intracerebral hemorrhage was associated with the severity of hemorrhage and poor clinical prognosis. Fujiki et al.[24] analyzed the GPR index in patients with subarachnoid hemorrhage. They reported that calculating glucose and potassium values together as GPR is more useful in evaluating the prognosis of this disease, rather than calculating these values separately.

In our study, we aimed to demonstrate the predictive ability of the GPR index for in-hospital mortality in patients diagnosed with AMI, by utilizing Troponin, NLR and PLR indexes that have been previously studied in this field, as well as lactate values that increase in the case of hypoxia. While the similarity of gender in demographic characteristics reduced bias formation a bit, the age factor showed a significant difference. Troponin levels were higher in fatal AMI in group comparison. Again, Lactate, NLR, and PLR were found to be high in the fatal AMI group. GPR showed a very strong increase in the fatal AMI group like troponin and lactate. In the diagnostic value analysis of the fatal AMI group compared to the non-fatal AMI group, Lactate showed the strongest potential. GPR showed a stronger diagnostic value than troponin.

Limitations

There are several limitations to this study. This study was initially planned as a retrospective cohort study. Therefore, we could not obtain data to compare insulin, glucagon, corticosteroid, insulin, and catecholamine levels with GPR, as well as HbA1c levels. The analysis was performed with a limited sample size at a single center. Despite all limitations, this is the first study to investigate the relationship between GPR and in-hospital mortality of AMI and will shed light on prospective studies in the future. The efficacy of GPR can be evaluated more clearly with prospective and multicenter studies by adding a control group.

CONCLUSION

GPR showed a strong increase in the fatal AMI group, consistent with Troponin, Lactate, and NLR. Additionally, GPR showed a stronger diagnosis than Troponin and NLP. GPR as a new, inexpensive biomarker may be useful in predicting in-hospital mortality of fatal and non-fatal AMI. However, it is weaker than Lactate but better than Troponin.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of Health Ministry of Turkish Republic Konya City Hospital Institution's Ethics Committee (Date: 05.01.2023, Decision No: 01-21).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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