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Original Research

Glucose-to-potassium ratio: A novel index associated with the clinical status in acute coronary syndrome patients

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Abstract
Aim: Acute coronary syndrome is the foremost cause of death in the world. Hyperglycemia and hypokalemia have been found to be associated with poor prognosis in ACS. In this study, we aimed to assess the diagnostic value of GPR in ACS.
Material and Methods: The study was designed as a retrospective cross-sectional clinical cohort study of patients with ACS. A total of 169 participants were enrolled in the research and divided into two groups: ACS (n:88) and Control (n:81). GPR was calculated by dividing serum glucose by potassium levels and its results were compared with Troponin, WBC, and NEU.
Results: Troponin was measured as 2261.76±3629.42 in the ACS group and found to be higher than in the Control group (4.8±3.11) (p=0.001). WBC (100±83,5 to 30,9±42,7mg/L; p=0,0001) and Neutrophil (49,5±11,9 to 34,8±7,3 mm Hg; p=0,0001) were found to be increased in the ACS group. GPR strongly increased in the ACS group compared to controls (25.61 to 24.15; p=0.001). GPR showed stronger diagnostic value (AUC: 0.97; p=0.001; Sensitivity: %92; Specificity: %86; Cut-off: 24.09).
Discussion: GPR as a novel and cheap marker, which can be useful for the diagnostic differentiation of ACS, but weaker than troponin and better than WBC and Neutrophil count.

Keywords
Acute Coronary Syndrome, Glucose-to-Potassium Ratio, WBC, Neutrophils

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Introduction

Acute coronary syndrome (ACS) is the main cause of death in the world. ACS can be defined as a spectrum between unstable angina and acute myocardial infarction. In acute coronary syndrome, coronary plaque ruptures and a platelet-rich thrombus forms. Coronary blood flow in the myocardium decreases and myocardial ischemia develops. The severity and duration of the imbalance between oxygen supply and demand results in reversible myocardial ischemia (unstable angina) or irreversible myocardial damage (AMI) [1, 2].

Many studies have shown that hyperglycemia is a major problem in critically ill patients, even if they are not diabetic. Epidemiological studies have shown that 25-50% of hospitalized acute coronary syndrome patients have hyperglycemia. Studies have shown that the prognosis is different between diabetic and non-diabetic patients with hyperglycemia during acute coronary syndrome. It has been observed that the frequency of adverse events is higher in diabetics with hyperglycemia in those diagnosed with ACS than in those without diabetes mellitus [3-5].

In the case of acute coronary syndrome, increased sympathetic activity activates the sodium potassium pump, and this causes extracellular potassium to be taken into the cell, causing hypopotassemia [6]. Even mild hypopotassemia is associated with poor prognosis in those with cardiovascular disease. Hypopotassemia has been associated with poor prognosis in patients with heart failure. In patients hospitalized with acute myocardial infarction, ventricular arrhythmia and cardiac arrest rates were found to be higher in patients with hypopotassemia at admission [7, 8].

Hyperglycemia and hypopotassemia appear to be an important problem during acute coronary syndrome. Although many indices have been suggested recently to determine the severity of acute coronary syndrome, research continues on tests that will be useful in rapid, practical and prognostic determination. Recently, studies have been published showing that the glucose/potassium ratio, which is a new index, will be useful in many acute clinical situations [9]. In our study, we aimed to investigate whether the glucose/potassium ratio, which we think would be cheap, easy and prognostic, could be useful in determining the severity of acute coronary syndrome.

Material and Methods

Before starting, the study protocol was approved by the local ethics committee of our hospital (Date: 17/05/2021, No: 2021-10-21)

Study design

The study was designed as a retrospective cross-sectional clinical cohort study, which compared patients with ACS according to the ESC guidelines in the emergency department (n=88) with the control group (n=81).

The data of the participants that included demographic information (age and gender), medication use and previous illness were collected from the electronic medical health records.

Patients whose condition was caused by changes in glucose and potassium levels due to medication or comorbidities such as ischemic heart disease (11), diabetes diagnosis and related pharmaceuticals (19), acute kidney failure (5) and corrupted potassium levels as a result of previous medication (7) were excluded from this study.

Laboratory Data

All patients with chest pain underwent atraumatic venipuncture, and venous blood samples were tested, including glucose, potassium, cardiac troponins, and other blood components, EDTA tube was used in the process. The complete blood count measurement, including differential biochemical parameters was worked on autoanalyzers (Mindray BC 6800, China), Cobos 6000 (Roche Diagnostics, USA), respectively. Glucose Potassium Ratio was determined using MS Excell by dividing the glucose level by the potassium level.

Statistical Analyses

SPSS (Statistical Package for the Social Sciences) 24.0 program was used for statistical analysis. While evaluating the study data, the Mann-Whitney U test was used in the two-group comparisons of the descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, Maximum), as well as an independent sample t, and also the Mann- Whitney U test was used for non-normally distributed parameters in the comparison of two groups. One Way Anova test was used in comparisons of three or more normally distributed groups, and the Kruskal-Wallis test was used in comparisons of three or more groups that did not show a normal distribution. The Bonferroni correction test was used in cases where there was a difference between the groups. ROC CURVE test was used to calculate the sensitivity and specificity values according to the groups (cut-off). Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

Results

In the demographic evaluation of the patients, there was no difference in main factors such as age and gender, as shown in Table-1. Thus, it was accepted that demographics did not have a biased effect on the study (Table-1).

Total cholesterol values and LDL values did not show statistically significant differences between the groups ($p>0.05$).

The glucose/potassium ratio shows statistically significant differences between the groups ($p=0.001$; $p<0.01$). According to the pairwise comparisons, it was found that the glucose/potassium values of the control group were lower than those in the Non-ST myocardial infarction (NSTEMI) ($p=0.001$) group and those in the ST elevation myocardial infarction (STEMI) ($p=0.001$) group.

Table 1. Demographic Information

		n	%
Gender	Male	87	51.5
	Female	82	48.5
Group	STEMI	41	24.3
	NON-STEMI	47	27.8
	CONTROL	81	47.9
Hypertension	No	90	53.3
	Yes	79	46.7
Hyperlipidemia	No	119	70.4
	Yes	50	29.6

HDL values showed statistically significant differences between the groups (p=0.001; p<0.01). According to the pairwise comparisons, it was found that HDL values were lower in the control group, NSTEMI (p=0.008) group and STEMI (p=0.007) group (Table-2).

Troponin values showed statistically significant differences between the groups (p=0.001; p<0.01). According to the paired comparisons, it was found that those in the control group had lower troponin values than those in the non-st (p=0.001) group and those in the st (p=0.001) group. It was found that those in the non-st group had lower troponin values than those in the st group (p=0.001) (Table-3).

Total cholesterol values did not show statistically significant difference between the groups (p>0.05).

Glucose/potassium values show statistically significant differences between the groups (p=0.001; p<0.01). Glucose/potassium values of those with acute coronary syndrome (ACS) were found to be higher than in the control group (Figure-1).

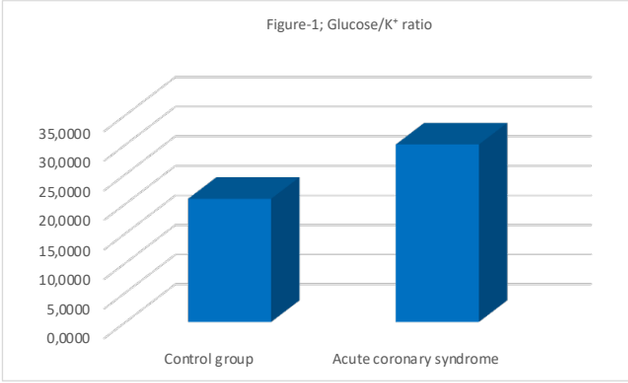

Figure 1. Glucose-to-potassium ratio between groups

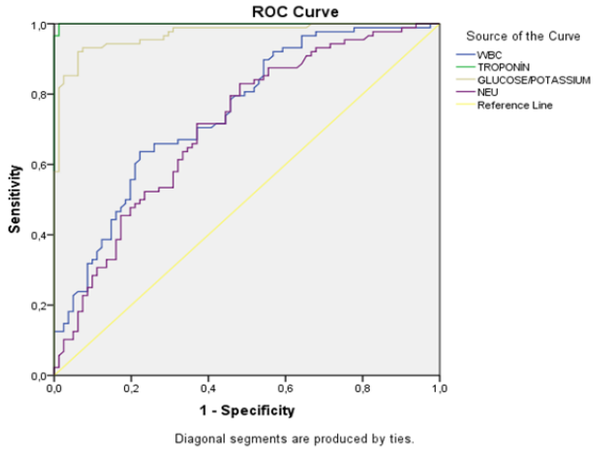

Figure 2. Receiver operating characteristic curve of GPR for predicting acute coronary syndrome

HDL values show statistically significant differences between the groups (p=0.001; p<0.01). HDL values of those in the ACS groups were found to be lower than in the control group.

LDL values differed statistically significantly between the groups (p=0.047; p<0.05). LDL values of those in the ACS groups were found to be higher than in the control group.

Troponin values showed statistically significant differences according to the groups (p=0.001; p<0.01). Troponin values of those in the ACS groups were found to be higher than in the control group.

Cut-off according to Glucose/Potassium ratio

Sensitivity and specificity values are calculated for the positivity limit (cut-off). The value with the highest specificity rate is determined as the cut off value (Figure-2). The cut-off value in determining the diagnosis according to the glucose/potassium ratio was 24.09 with a sensitivity of 92% and specificity of 86%.

Discussion

In our study, we determined that the glucose/potassium ratio would be useful in determining the severity of acute coronary syndrome. Our study is regarded as the first study conducted when looking at the available literature. Stress-induced hyperglycemia (SIH) is observed in many critical clinical situations. Hyperglycemia is a common clinical picture in the stress environment of acute coronary syndrome [10]. As a result of many observational studies, it has been observed that hyperglycemia is frequently observed in patients hospitalized with acute coronary syndrome, even without a diagnosis of diabetes [11, 12].

Table 2. Evaluation of Troponin, Glucose/Potassium, Total Cholesterol, HDL and LDL Differences by Groups

	STEMI (n=41)		NON-STEMI (n=47)		Control (n=81)		p
	Mean±Sd	Min-Max (Median)	Mean±Sd	Min-Max (Median)	Mean±Sd	Min-Max (Median)	
Glucose/Potassium	31.16±5.95	22.51-46.75 (31.06)	29.0±4.77	20-45.81 (28.54)	20.83±2.46	13.83-28.18 (20.91)	0.001**
Total cholesterol	212.85±38.41	130-282 (215)	211.55±42.01	120-313 (214)	199.42±49.03	110-417 (191)	0.183
HDL	41.44±9.04	21-62 (41)	41.63±10.99	23-67 (41)	48.07±12.55	23-84 (45)	0.001**
LDL	136.24±38.55	72-197 (140)	135.85±34.77	66-211 (140)	123.67±43.69	51-311 (114)	0.139
Troponin	3945.48±4531.95	19.9-23010 (2340)	792.99±1524.14	24.4-9436 (423)	4.8±3.11	1.2-28 (4.26)	0.001**

Table 3. Evaluation of Troponin Difference by Groups

	STEMI (n=41)		NON-STMI (n=47)		Control (n=81)		[b]p
	Mean±Sd	Min-Max (Median)	Mean±Sd	Min-Max (Median)	Mean±Sd	Min-Max (Median)	
Troponin	3945.48±4531.95	19.9-23010 (2340)	792.99±1524.14	24.4-9436 (423)	4.8±3.11	1.2-28 (4.26)	0.001**

[b]Kruskal- Wallis Test, **p<0.01

Although SIH is frequently associated with adverse outcomes in patients admitted to the hospital with ACS, there is still no clear definition for SIH. In the literature, blood glucose measured in the first 24 hours in patients hospitalized with ACS is the recommended method for sanitation, but there is still no common consensus on this issue. The cut-point used for hyperglycemia in patients presenting with ACS varies from study to study. The American Heart Association recommends that a cut-point blood glucose value above 140 mg/dl can be taken under certain conditions. This recommendation of the American Heart Association is based on retrospective observational studies [13].. In an observational study by Kosiborod et al, 30-day and 1-year mortality increased significantly in non-diabetic patients with acute coronary syndrome at glucose levels of 110-140 mg/dl, whereas mortality increased at blood glucose levels >240 mg/dl in diabetics [14]. According to the results of the CARDINAL study, 30-day mortality increased significantly in patients with blood glucose >140 mg/dl at admission [15]. In the study by Capes et al., in their meta-analysis, which included 15 studies, in-hospital death rate was found to be 3.9 times higher in non-diabetics with blood glucose values >110 at admission. On the other hand, in-hospital mortality increased when the blood glucose level was >180 in diabetics [10]. When we look at the observational studies, hyperglycemia has been found to be associated with adverse events in patients presenting with acute coronary syndrome, but the cut-point could not be clearly defined, and the cut-point was seen to differ significantly between diabetic and non-diabetic patients [16].

Serum potassium level is regulated by the ATP-Na/K pump on the cell surface. An increase in the level of stress hormones in acute clinical events activates this pump, and potassium entry from extracellular to intracellular increases [17]. During an acute coronary syndrome, increased stress hormones and consequent hyperglycemia, increased intracellular K uptake, and insulin secretion will have clinical consequences. GPR, a new index recently described, has been associated with many clinical conditions [18]. Matano et al. found a strong relationship between GPR and vasospasm in patients with cerebral infarction [19]. In a study of patients with subarachnoid hemorrhage, GPR with both rather than glucose or potassium alone showed better bleeding status [20].

In our study, we aimed to investigate whether the GPR differs between the patients with acute coronary syndrome and the control group, considering the troponin, ck and ckmb levels. The similarity of the two groups decreased the bias rate. As expected in our study, trop, ck and ckmb levels were significantly higher in the axis group. GPR level was found to be high in the acute coronary syndrome group in correlation with trop, ck and ckmb levels. Our study showed that GPR is an inexpensive and easy indicator of acute coronary syndrome, which will both shed light on future prospective studies and guide the treatment approach.

Our study had some limitations. First of all, the study was designed retrospectively. HBA1c, insulin, glucagon hormone levels and cortisol levels of the patients included in the study were not checked, which can be counted as a limitation. The number of patients included in the study was limited and the study was conducted in a single center. Despite all these limitations, it is important because it is the first study to investigate the relationship between GPR and ACS. Our study will shed light on future multicenter and prospective studies.

Conclusion

In our study, GPR was found considerably higher in the group of patients with ACS, alike Troponin, WBC, NEU. GPR was more meaningful than WBC, NEU and weaker than Troponin as a diagnostic value. We can conclude that GPR may be a new diagnostic parameter in the cases of ACS after further investigation.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Reindl M, Reinstadler SJ, Feistritzer H-J, Mayr A, Klug G, Marschang P, et al. Acute myocardial infarction as a manifestation of systemic vasculitis. Wiener Klinische Wochenschrift. 2016;128(21):841-3.

2. Haasenritter J, Stanze D, Widera G, Wilimzig C, Abu Hani M, Sönnichsen AC, et al. Does the patient with chest pain have a coronary heart disease? Diagnostic value of single symptoms and signs–a meta-analysis. Croat Med J. 2012;53(5):432-41.

3. Shahid M, Zarif HMA, Farid MS, Abid MS, Akhtar B, Khan MR. Prognostic value of hyperglycemia on admission on in-hospital outcomes in patients presenting with ST-elevation myocardial infarction. Cureus. 2020;12(2). DOI: 10.7759/cureus.7024.

4. Ding XS, Wu SS, Chen H, Zhao XQ, Li HW. High admission glucose levels predict worse short-term clinical outcome in non-diabetic patients with acute myocardial infarction: a retrospective observational study. BMC Cardiovascular Disorders. 2019;19(1):1-9.

5. Kim EJ, Jeong MH, Kim JH, Ahn TH, Seung KB, Oh DJ, et al. Clinical impact of admission hyperglycemia on in-hospital mortality in acute myocardial infarction patients. Int J Cardiol. 2017; 236:9-15.

6. Brown M, Brown D, Murphy M. Hypokalemia from beta2-receptor stimulation by circulating epinephrine. N Eng J Med. 1983;309(23):1414-9.

7. Goyal A, Spertus JA, Gosch K, Venkitachalam L, Jones PG, Van den Berghe G, et al. Serum potassium levels and mortality in acute myocardial infarction. JAMA. 2012;307(2):157-64.

8. Nordrehaug J, Johannessen K, Von Der Lippe G. Serum potassium concentration as a risk factor of ventricular arrhythmias early in acute myocardial infarction. Circulation. 1985; 71(4):645-9.

9. Shibata A, Matano F, Saito N, Fujiki Y, Matsumoto H, Mizunari T, et al. Serum glucose-to-potassium ratio as a prognostic predictor of severe traumatic brain injury. J Nippon Med Sch. 2020; 88(4):342-6.

10. 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. The Lancet. 2000;355(9206):773-8.

11. Kosiborod M, Inzucchi SE, Spertus JA, Wang Y, Masoudi FA, Havranek EP, et al. Elevated admission glucose and mortality in elderly patients hospitalized with heart failure. Circulation. 2009;119(14):1899-907.

12. Kojima T, Hikoso S, Nakatani D, Suna S, Dohi T, Mizuno H, et al. Impact of hyperglycemia on long-term outcome in patients with ST-segment elevation myocardial infarction. Am J Cardiol. 2020;125(6):851-9.

13. Deedwania P, Kosiborod M, Barrett E, Ceriello A, Isley W, Mazzone T, et al. 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. 2008;117(12):1610-9.

14. Kosiborod M, Rathore SS, Inzucchi SE, Masoudi FA, Wang Y, Havranek EP, et al. Admission glucose and mortality in elderly patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation. 2005;111(23):3078-86.

15. Goyal A, Mahaffey KW, Garg J, Nicolau JC, Hochman JS, Weaver WD, et al. Prognostic significance of the change in glucose level in the first 24 h after

acute myocardial infarction: results from the CARDINAL study. Eur Heart J. 2006;27(11):1289-97.
16. Hao Y, Lu Q, Li T, Yang G, Hu P, Ma A. Admission hyperglycemia and adverse outcomes in diabetic and non-diabetic patients with non-ST-elevation myocardial infarction undergoing percutaneous coronary intervention. BMC Cardiovascular Disorders. 2017;17(1):1-9.
17. Sadiq SMM, Dakhil MA, Dakhil ZA. Effect of Diabetes on Laboratory Markers in Patients with Non-ST Elevation Acute Coronary Syndromes. J Phys Conf Ser. 2021;1818(1):012040. DOI: 10.1088/1742-6596/1818/1/012040
18. Boyuk F. The Predictor Potential Role of the Glucose to Potassium Ratio in the Diagnostic Differentiation of Massive and Non-Massive Pulmonary Embolism. Clinical and Applied Thrombosis/Hemostasis. 2022;28. DOI:10.1177/10760296221076146
19. Matano F, Fujiki Y, Mizunari T, Koketsu K, Tamaki T, Murai Y, et al. Serum glucose and potassium ratio as risk factors for cerebral vasospasm after aneurysmal subarachnoid hemorrhage. J Stroke Cerebrovasc Dis. 2019;28(7):1951-7.
20. Fujiki Y, Matano F, Mizunari T, Murai Y, Tateyama K, Koketsu K, et al. Serum glucose/potassium ratio as a clinical risk factor for aneurysmal subarachnoid hemorrhage. J Neurosurg. 2017;129(4):870-5.

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