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The leuko-glycemic index can predict multivessel disease in the elderly acute myocardial infarction population? a retrospective cohort study

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ABSTRACT

Aims: Cardiovascular diseases are still the leading cause of death, as the cause of approximately 30% of all deaths in the world and half of all deaths due to cardiovascular diseases also consist of individuals aged 70 and older. The leukoglycemic index (LGI) is a new parameter associated with mortality, complication, and prognosis in cardiovascular diseases. It can be applied easily at the bedside, has a low cost, and consists of a combination of leukocytes and glucose. In our study, we aimed to evaluate the predictive effect of leukoglycemic index on multivessel disease in elderly patients over 65 who were hospitalized with acute myocardial infarction.

Methods: In our retrospective cohort study, patients over 65 who were hospitalized with the diagnosis of acute myocardial infarction were included. LGI was calculated with the formula: blood glucose × white blood cell/1000. All datas about patients were collected from the electronic hospital information system, patient files and our hospital's archive.

Results: The patients were divided into two groups: single-vessel disease and multivessel disease. The laboratory parameters of the patients were compared, and LGI (1532.5 (577.7-3770.3) vs 2077.9 (646.6-5301); p<0.001) were found to be significantly different between the two groups. According to unadjusted univariate log regression analysis, LGI was statistically significant in predicting multivessel disease (OR: 1.724, 95% CI: (1.222-2.432), p=0.002). After adjusting the model by adding clinically and statistically significant variables, LGI remained an independent predictor of multivessel disease (OR: 1.599, 95% CI (1.086-2.357), p=0.018). The discrimination ability of LGI was analyzed with ROC curve analysis. The LGI AUC value was 0.619 (95% Cl, 0.544-0.695, p=0.003).

Conclusion: Our study showed that high LGI is an independent predictor of multivessel coronary artery disease in elderly patients with acute myocardial infarction.

Keywords: Blood glucose, coronary artery disease, elderly, leukocyte, myocardial infarction

INTRODUCTION

Cardiovascular diseases are still the leading cause of death, as the cause of approximately 30% of all deaths in the world and half of all deaths due to cardiovascular diseases also consist of individuals aged 70 and older.[1]

While the EU population over the age of 65 was about 12% in the 1950s, according to recent data, it is seen that the proportion of individuals over the age of 65 is about 19.2% today, and it is estimated that this will reach 36% in 2050.[2,3] When the data and statistics are analyzed, the elderly population will increase even more over the years, and we will encounter the elderly patient population more. More studies on the elderly population, where diagnosis and treatment management are difficult, comorbidity is high, and relatively few studies are available, can be considered the main factor in creating diagnosis, treatment and follow-up algorithms.

The leukoglycemic index (LGI) is a new parameter associated with mortality, complications, and prognosis in cardiovascular disease. It can be applied easily at the bedside, has a low cost, and consists of a combination of leukocytes and glucose.[4-7] For the first time, 101 ST-elevated patients, LGI was evaluated by Quiroga Castro et al.[7] and was shown to be independently associated with both in-hospital mortality and complications. Systematic review and meta-analysis of eleven studies by Roxana Sadeghi et al.[4] stated that LGI is independently associated with mortality and complications after acute myocardial infarction. Identifying patients at high risk

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for coronary artery disease (CAD) can guide physicians in terms of preventive measures, follow-up planning and treatment intensity. For this purpose, many studies have been conducted on biomarkers and scoring. Our study was designed to determine the prognostic value of this index in different cardiovascular patient populations.

In our study, we aimed to evaluate the predictive effect of the leukoglycemic index on multivessel disease in elderly patients who were hospitalized with acute myocardial infarction.

METHODS

The study was initiated with the approval of the Kutahya Health Science University Non-interventional Clinical Researches Ethics Committee (Date: 10.07.2023, Decision No: 2023/08). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In our retrospective cohort study, patients over 65 who were hospitalized with the diagnosis of acute myocardial infarction (AMI) and underwent coronary angiography between January 2022 and June 2023 were included.

Patients with chronic coronary syndrome, active malignancy, active infectious disease, severe hepatic and renal failure, active or recent internal bleeding, and other significant comorbidities were excluded from the study. As a result, 22 patients were excluded (Figure 1). The patient's data were analyzed retrospectively through the hospital's electronic data information system and patient files.

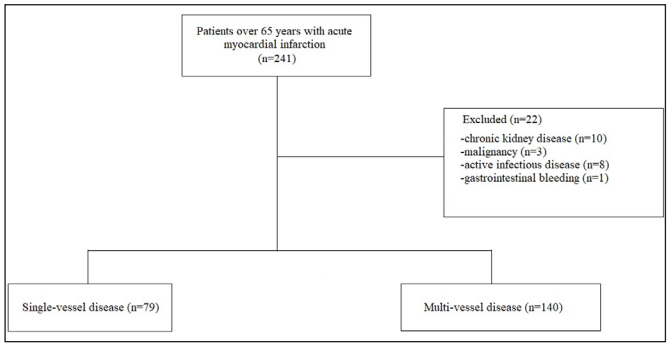

Figure 1. Diagram of the patient flowchart

We analyzed peripheral venous blood samples from the patients in the hematology laboratory, and complete blood count parameters were calculated by an automated blood counter (Beckman Coulter, Brea, CA). Blood glucose levels, urea, creatinine, glomerular filtration rate, albumin, alanine aminotransferase, total cholesterol, high-density lipoprotein, low-density lipoprotein, triglyceride, troponin I were analyzed in the biochemistry laboratory for all patients on admission.

Demographic characteristics, medical history and clinical and laboratory data of patients were recorded. Echocardiographic and angiographic images were analyzed from the hospital's electronic imaging system, patients files and our hospital's archive.

Multivessel coronary artery disease was defined as 50% or more stenosis in at least two coronary arteries. The patients were divided into multivessel and single coronary artery disease. LGI was calculated with the formula: blood glucose x white blood cell/10^3.[7]

Statistical Analysis

We analyzed the data with SPSS, version 21.0 (IBM). The normality of distribution for parametric data was evaluated with the Shapiro-Wilks test. Levene's test analyzed the homogeneity of the data. For continuous variables with a normal distribution, means accompanied by standard deviations (±SD) were employed, while for variables without a normal distribution, minimum and maximum values were utilized. The differences between the categorical variables of the groups were analyzed using the chi-square test. The differences in the numerical variables for the independent groups were evaluated with the t-test or Mann-Whitney U test.

The discriminative abilities and cut-off points of the leuko-glycemic index in predicting multivessel disease were compared using the area under the ROC curve. Univariate and multivariate logistic regression models were used to evaluate the independent association of the leuko-glycemic index with multivessel disease; odds ratios are reported with their respective 95% confidence intervals. Clinically and statistically significant variables were included in the variants in the logistic regression analysis. The level of significance was set at $p<0.05$.

RESULTS

Our study included 219 patients, 72 (32.9%) women and 147 (67.1%) men, hospitalized with acute miyocardial infarction and underwent coronary angiography. According to the study design, all patients were over 65, and the mean age was 71.2±5.7 years. The patients were divided into two groups: single-vessel disease and multivessel disease.

It was observed that a history of hypertension (HT) (32.9%, vs. 47.9%; p=0.032) and diabetes mellitus (DM) (27.8%, vs. 44.3%; p=0.016) was more frequent in multivessel disease. The laboratory parameters of the patients were compared, and total cholesterol (172.2 (72-291) vs 185.1 (78-319); p= 0.049) triglyceride (114.3 (41-533) vs 141.9 (42-533); p=0.030) and LGI (1532.5 (577.7-3770.3) vs 2077.9 (646.6-5301); p<0.001) were found to be significantly different between the two groups. Baseline clinical, demographic and laboratory characteristics of the study population according to the multivessel disease are shown in Table 1. It was observed that gender and age

were not associated with multivessel disease over 65 years of age. There were no significant differences in AMI type, albumin, alanine aminotransferase, white blood cell, hemoglobin, platelet, and troponin parameters between the two groups on admission.

According to univariate logistic regression analysis, LGI was statistically significant in predicting multivessel disease (Odds Ratio: 1.724, 95% CI: (1.222-2.432), p=0.002). After adjusting the model by adding clinically and statistically significant variables (HT, total cholesterol, DM, LGI), LGI was still an independent predictor of multivessel disease (Odds Ratio: 1.599, 95%CI: (1.086-2.357), p=0.018) (Table 2).

The discrimination ability of LGI was analyzed with ROC curve analysis. The LGI AUC value was 0.619 (%95 Cl, 0.544-0.695, p=0.003). The cut-off value for LGI was 1471.65, with sensitivity of 55.7% and specificity of 55.7% (Figure 2).

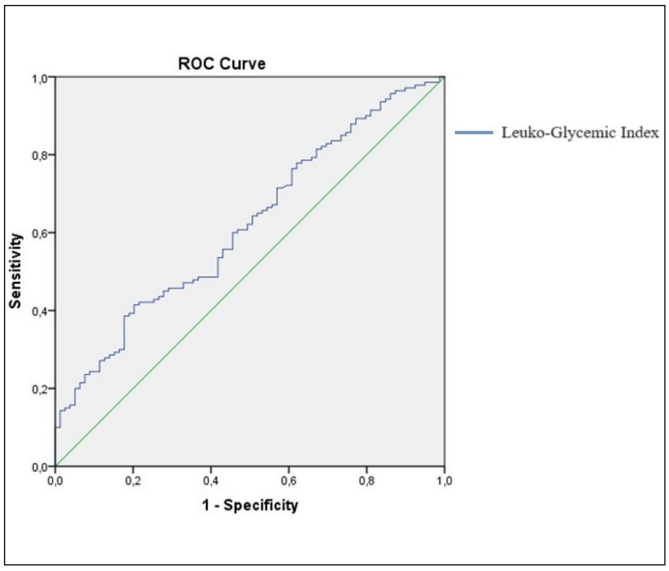

Figure 2. Receiver-operating characteristic (ROC) curve analysis plot to determine the cut-off value of LGI in the prediction of multivessel diseae. AUC: 0.619 (95% Cl, 0.544-0.695, p=0.003)

Table 1. Baseline and laboratory characteristics according to single vessel vs multivessel coronary artery disease.

Characteristics	Single-vessel CAD (n=79)	Multi-vessel CAD (n=140)	p value
Age (years), mean ± SD	71.4 ± 5.6	71.2 ± 5.8	0.796
Sex, male %	68.4	66.4	0.771
Diabetes mellitus, %	27.8	44.3	0.016
Hypertension, %	32.9	47.9	0.032
Prior cerebrovascular event, %	0	5.6	0.306
Peripheral artery disease, %	2.5	1.4	0.826
MI type (STEMI), %	49.4	45	0.534
Ejection fraction (%), median (min-max)	48.4 (25-65)	47.3 (25-70)	0.521
Serum creatinine (mg/dl), median (min-max)	1.04 (0.3-1.89)	1.06 (0.55-2.0)	0.803
Total cholesterol (mg/dl), median (min-max)	172.2 (72-291)	185.1 (78-319)	0.049
LDL-C (mg/dl), median (min-max)	110 (25-198)	117.2 (49-251)	0.178
HDL-C (mg/dl), median (min-max)	42.6 (18-79)	41.2 (10-73)	0.385
Triglyceride (mg/dl), median (min-max)	114.3 (41-533)	141.9 (42-533)	0.030
WBC (×10³ µl), median (min-max)	10.4 (5.3-19.7)	10.8 (5.3-26.4)	0.417
Hemoglobin (g/dl), median (min-max)	13.5 (6.7-18.8)	13.4 (9.3-17.6)	0.646
Platelet (×10³ µl), median (min-max)	243.5 (94-566)	235.8 (60-630)	0.475
Neutrophyl (×10³ µl), median (min-max)	7.7 (2.7-18)	7.8 (0.4-23.1)	0.853
ALT (U/L), median (min-max)	31.8 (8-360)	32.2 (6-410)	0.951
Albumin (g/L), median (min-max)	40.7 (28-49.2)	39.2 (28-47.7)	0.871
Troponin (ng/ml), median (min-max)	13205 (0.40-95000)	4508.7 (0.50-82000)	0.142
LGI, median (min-max)	1532.5 (577.7-3770.3)	2077.9 (646.6-5301)	<0.001

ALT, alanine aminotransferase; CAD, coronary artery disease; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; LGI, leuko-glycaemic index; MI, myocardial infarction; STEMI, ST elevated myocardial infarction; TG, triglyceride; WBC, white blood cell

Table 2. Univariate and multivariate regression analysis of significant parameters for multivessel disease

Variables	Univariate		Multivariate	
	OR (95% Cl)	p value	OR (95% Cl)	p value
HT	1.870 (1.053-3.320)	0.033	1.729 (0.930-3.215)	0.084
DM	2.059 (1.137-3.731)	0.017	1.100 (0.545-2.218)	0.790
Total cholesterol	1.006 (1.000-1.013)	0.054	1.006 (0.999-1.013)	0.074
LGI	1.724 (1.222-2.432)	0.002	1.599 (1.086-2.357)	0.018

DM, diabetes mellitus; HT,hypertension; LDL, low density lipoprotein; LGI, leuko-glycaemic index.

DISCUSSION

In this study, we showed that leukoglycemic index is an independent predictor of multiple coronary artery disease in elderly patients who are hospitalized with the diagnosis of AMI.

The LGI consists of two parameters: leukocyte count and blood glucose level on admission. Leukocytes are one of the primary mediators of inflammation and are also used in the clinic as a marker of inflammation. It has been shown that peripheral leukocyte count is closely related to in-hospital mortality, cardiogenic shock, and heart failure in patients with acute myocardial infarction.[8,9] With increasing evidence over the years, it is known that chronic inflammation also has a main role in atherosclerosis. Various inflammatory biomarkers, such as leukocytes and C-reactive protein, have been used to predict the risk of coronary artery disease.[10,11] At the same time, previously published studies have shown that the total leukocyte count is also independently associated with the presence and severity of coronary artery disease and plaque calcification.[12,13]

During acute stress, glucose metabolism is affected by inflammatory mediators, independent of diabetes mellitus, and hyperglycemia occurs.[14] Stress hyperglycemia is defined by the American Diabetes Association (ADA) as having a random glucose level higher than 140 mg/dl in hospitalized patients at any time. Hyperglycemia, which can be seen as an inflammatory response regardless of diabetes mellitus, is seen in 58% of patients with acute coronary syndrome.[15] A previous study showed a significant association between hyperglycemia and high leukocyte count in AMI patients.[16] Admission hyperglycemia has been shown in many studies to be associated with both in-hospital and long-term increased adverse outcomes in ACS patients, independent of diabetes mellitus.[14,17,18]

In the study published by Ling-Yao Qi et al.[5] 1256 AMI patients from multiple centers were included in the observational study. The patients were divided into two groups: diabetic and non-diabetic. Optimal cut-off values were determined as 3593 mg/dl mm^3 for diabetics and 1402 mg/dl mm^3 for non-diabetics. The study concluded that LGI is an independent predictor of all-cause mortality in hospital and MACE at follow-up in nondiabetic patients, but not in diabetics. In our study, diabetic and nondiabetic patients were also included. It was shown that history of diabetes mellitus is not a independent predictor, but LGI is an independent predictor for multivessel disease in the elderly population.

In the study of Oguz Kilic et al.[6] the relationship between LGI and the severity of CAD in patients with chronic coronary syndrome has been investigated. The severity of CAD was evaluated by the Gensini score. It has been shown that LGI is an independent predictor of the severity of CAD, and LGI was correlated with the Gensini score in patients with chronic coronary syndrome. In addition, according to the results, it was observed that age was an independent predictor. In our study, we evaluated the severity of coronary artery disease in elderly AMI patients and observed that while age was not significant, LGI was an independent predictor.

Despite the significant reduction of mortality in coronary artery disease with the development of new antiaggregant drugs, mortality-reducing treatments, new stent technologies, and techniques, acute coronary syndromes (ACS) still rank first in the causes of death in worldwide.[19] Cardiovascular diseases account for 82% of the causes of death in patients over 65.[20] However, because studies on elderly patients are mostly subgroup analyses and few randomized studies, the data on elderly patients can still be considered insufficient.[21,22] It is known that age alone is an important risk factor for cardiovascular diseases. Furthermore, it has also been stated that individuals over 60 can be considered very high-risk.[23] Age is also directly related to ACS patients' mortality, which increases sharply, especially after 70.[21,24] In addition, coronary artery disease is more often accompanied by multi-vessel disease, left main coronary artery disease, coronary calcification, and heart failure in elderly patients.[1,25,26] Other cardiac problems that occur with increasing age are structural and functional changes such as myocyte loss and left ventricular hypertrophy, increased fibrocalcification in the valves, cell loss in the sinoatrial node, changes in systolic and diastolic functions and volumes.[2,27,28]

The increase in comorbidities such as hypertension, chronic kidney diseases, neurocognitive diseases with advancing age, and the more frequent atypical clinical presentation cause errors in the diagnosis process and more defensive treatment approaches against elderly fragile patients. 80% of people over 65 have at least one chronic condition, and 68% have two or more chronic diseases. It should be known that elderly patients are also not homogeneous. Therefore their prognosis is different, and their life expectancy may change.[1,2] The treatment process in elderly patients also requires a multidisciplinary approach due to polypharmacy, drug interactions, side effects, incompatibilities, cognitive disorders, and organ failures.

In the registry published by Kochar et al.[29] AMI patients over 65 were evaluated, and 8-year mortality was found to be 65%. It has even been reported that the long-term mortality of patients who lived for one year after index MI coronary revascularization exceeded 45%. In the Global Registry of Acute Coronary Events (GRACE), it has been

reported that although ST-elevation myocardial infarction is observed more frequently in the younger age population, the frequency of non-ST elevation myocardial infarction increases with increasing age. In the follow-up, it was observed that bleeding complications, cardiogenic shock, and in-hospital mortality were higher in elderly patients.[30]

The multivessel disease has been defined as 50% or more in at least two coronary arteries and associated with a poor prognosis in ACS patients. Although the issue of multiple coronary artery revascularization strategy in ACS patients is controversial, evaluation should be made according to patient and lesion characteristics, and gradual total revascularization for ischemic lesions is recommended.[22,31] In Angiocardio registry published by Cantarelli et al.[32] 16320 patients were analyzed, and independent risk factors in multivessel coronary artery disease (more than 50% stenosis in more than one coronary artery) were evaluated. Age, diabetes mellitus and chronic kidney disease were stated to be the most substantial risk factors for multivessel coronary artery disease.

Considering the above studies, combining leukocyte and blood glucose levels as a new parameter with the prevalence of multivessel coronary artery disease in patients with AMI is reasonable and feasible. Especially in elderly patients with insufficient studies, these scores can give an idea about patient prognosis, follow-up, and even treatment intensity, and a strategy can be planned.

Limitations

There are several limitations of this study. Initially, the study was designed as a retrospective and single-center study. Our number of patients is relatively insufficient. There is a need for more patient numbers and prospective studies on this subject. Another limitation is that the medication information of patients cannot be accessed retrospectively, and the proBNP, CRP, etc. levels of patients cannot be included in the study due to the fact that they are not routinely analyzed during hospitalization. The results cannot be generalised, considering the number of patients and their data.

CONCLUSION

Our study showed that high LGI is an independent predictor of the multivessel coronary artery disease in elderly patients with AMI.

The use of this inexpensive and simple index in combination with other cardiac tests in elderly patients may also provide some information about the severity of coronary artery disease. Prospective studies are needed to show the cardiovascular prognostic relationship between LGI and multiple coronary artery disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Kütahya Health Sciences University Non-interventional Clinical Researches Ethics Committee (Date: 10.07.2023, Decision No: 2023/08).

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 the authors declare 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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