CorSalud 2019 Jan-Mar;11(1):21-29

CorSalud

Cuban Society of Cardiology

Original Article

Cardiocentro Ernesto Che Guevara Santa Clara Cuba

The leucoglycaemic index is a predictor of all-cause mortality per year in Cuban patients with ST-segment elevation acute myocardial infarction

David Padilla-Cueto[1,2]✉, MD; Halbert Hernández-Negrín[2,3], MD; José I. Ramírez-Gómez[1,2], MD; Arlenys Pérez-Valdivia[2,4], MD; Ana L. Cárdenas-Sánchez[2], MD; and Adrián Alfonso-Izquierdo[2], Std

[1] Servicio de Cardiología, Hospital Arnaldo Milián Castro. Villa Clara, Cuba.
[2] Universidad de Ciencias Médicas de Villa Clara. Villa Clara, Cuba.
[3] Servicio de Medicina Interna, Hospital Arnaldo Milián Castro. Villa Clara, Cuba.
[4] Departamento de Microbiología. Hospital Arnaldo Milián Castro. Villa Clara, Cuba.

Este artículo también está disponible en español

ARTICLE INFORMATION

Received: July 28, 2018
Accepted: August 27, 2018

Competing interests
The authors declare no competing interests

Acronyms
AMI: acute myocardial infarction
LGI: leuko-glycaemic index

✉ *D Padilla-Cueto*
Calle A #29, e/ C. Camajuaní y Circunvalación. Santa Clara 50300. Villa Clara, Cuba. E-mail address: davidpadillacueto@gmail.com

ABSTRACT

Introduction: The leuko-glycaemic index has been proposed as a prognostic marker of death in patients with acute myocardial infarction, but there is uncertainty surrounding its prognostic value to predict one-year mortality.
Objectives: The aim of this study was to determine the prognostic value of leuko-glycaemic index for one-year mortality in Cuban patients with ST-segment elevation myocardial infarction.
Method: The data were obtained from the medical records and all cause one-year deaths was the primary endpoint. The leuko-glycaemic index was calculated from measurements at admission. The patients were divided into leuko-glycaemic index tertiles to be evaluated. Receiver operating characteristics and Kaplan-Meier survival curves were performed. Cox regression model was used for all multivariable analysis.
Results: Three hundred and forty-four patients were assessed (median age, 68 years; 65.7% males; 25.6% diabetic). The mortality rate was 25.6%, being significantly higher in the upper tertile (55.7%, p<0.0001). The deceased patients presented a median of leuko-glycaemic index significantly higher than the survivors (2.18 and 1.34 respectively, p<0.0001). The area under the curve for leuko-glycaemic index was 0.715 and its cut-off value was 2.2. Any leuko-glycaemic index value higher than 2.2 was associated with significantly lower survival (177 vs. 309 days, p<0.0001) and it was an independent predictor of mortality (HR=3.56, CI 95%, 2.09-6.07, p<0.0001).
Conclusions: The leuko-glycaemic index is a good predictor for all cause one-year mortality in patients with ST-segment elevation myocardial infarction.
Keywords: Leuko-glycaemic index, Myocardial infarction, Mortality, Survival, Leukocytes, Blood glucose

El índice leucoglucémico es un predictor de mortalidad por todas las causas al año en pacientes cubanos con infarto agudo de miocardio con elevación del segmento ST

RESUMEN

Introducción: El índice leucoglucémico (ILG) ha sido propuesto como marcador

pronóstico de muerte en pacientes con infarto agudo de miocardio; sin embargo, no existe evidencia sobre su valor pronóstico al año.
Objetivo: El objetivo del estudio fue determinar el valor pronóstico del ILG en la mortalidad al año de pacientes cubanos con infarto agudo de miocardio con elevación del segmento ST.
Método: Los datos fueron obtenidos de las historias clínicas y el objetivo primario fue la muerte por todas las causas al año. El ILG se calculó con los valores al ingreso. Para el análisis se dividieron los pacientes en terciles de ILG, se construyeron curvas de características operativas del receptor y de supervivencia de Kaplan-Meier. Para el análisis multivariable se utilizó la regresión de Cox.
Resultados: Se analizaron 344 pacientes (mediana de edad, 68 años; el 65,7% masculino; un 25,6% diabéticos). La mortalidad fue de 25,6% y fue significativamente mayor en el tercil superior (55,7%; p<0,0001). Los pacientes fallecidos presentaron una mediana de ILG significativamente mayor que los sobrevivientes (2,18 y 1,34, respectivamente; p<0,0001). El área bajo la curva del ILG fue de 0,715 y el punto de corte: 2,2. Un valor de ILG mayor de 2,2 se asoció a una supervivencia significativamente menor (177 vs. 309 días; p<0,0001) y fue un predictor independiente de mortalidad (HR=3,56; IC 95%, 2,09-6,07; p<0,0001).
Conclusiones: El índice leucoglucémico es buen predictor de mortalidad al año, por todas las causas, en pacientes con infarto agudo de miocardio con elevación del segmento ST.
Palabras clave: Índice leucoglucémico, Infarto de miocardio, Mortalidad, Supervivencia, Leucocitos, Glucemia

INTRODUCTION

Cardiovascular diseases have progressively increased their presence throughout the world, in such a way that they have become the leading cause of mortality. Despite significant improvements in reperfusion strategies and medical therapy, acute myocardial infarction (AMI) remains associated with significant morbidity and mortality[1].

Inflammation plays an important role in the development of atherosclerotic disease and coronary thrombosis[2]. Previous studies have shown that elevated levels of inflammatory markers are associated with the severity of coronary disease and with a worse prognosis[3-5]. Despite the existence of novel markers (interleukins, C-reactive protein, homocysteine, natriuretic peptides, fibrinogen, among others), counting leukocytes and their differential components is a rapid, universal and inexpensive tool to establish both procedure and prognosis to be followed[6,7]. Moreover, hyperglycemia caused by an inflammatory and adrenergic response to ischemic stress is frequent and constitutes an independent prognostic factor of death and complications in acute coronary syndrome[8,9].

The association of these 2 parameters in the leuko-glycaemic index (LGI) has been proposed as a prognostic marker of in-hospital death and complications in AMI patients[10-13]. However, it is still necessary to reproduce such results in more studies, as well as to evaluate their significance after one year. Hence, the objective of this study was to determine the prognostic value of LGI in all-cause mortality per year in Cuban patients presenting with ST-segment elevation AMI.

METHOD

Study population

Patients admitted to the Hospital Universitario Arnaldo Milián Castro, Villa Clara (Cuba) were included, with a diagnosis of ST-segment elevation AMI in the period between January 2011 and December 2015. Those with presence of systemic hematological/ inflammatory infectious diseases, that may alter blood count, as well as patients with an unknown condition at the end of the follow-up (alive or deceased) were excluded.

Variables

The data were obtained from the medical records. The information regarding personal data, background (age, sex, smoking habit, hypertension, diabetes mellitus, previous AMI, atrial fibrillation, chest pain and heart failure), clinical and laboratory tests at admission (heart rate, systolic and diastolic blood pressure, Killip-Kimball classification, blood count,

neutrophils, lymphocytes, glycemia and creatinine), and coronary reperfusion treatment (thrombolysis, percutaneous coronary intervention or both). The percutaneous coronary intervention performed during admission was taken into account since in our center it is not performed as a primary way. Thrombolysis was performed with recombinant streptokinase.

Leuko-glycaemic index

For the calculation of LGI, we considered that the leucogram and blood glucose levels were performed at admission. The following formula LGI = (glycemia [mg/dl] × leukocytes [10^6/l])/1000 was used[10].

Definition of the event and follow-up

We defined as a dependent variable death from all causes of patients diagnosed with ST-segment elevation AMI during the 2011-2015 period. This information was obtained by combining a telephone follow-up survey 365 days after admission with data from the provincial mortality registry, from the Statistics Department of the Provincial Directorate of Public Health.

Ethical considerations

The study was approved by the Ethics Committee of the institution. The patients' personal data were not published and the principles established in the Declaration of Helsinki were followed.

Statistical analysis

The patients were divided into 3 groups according to the LGI tertiles. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of the quantitative variables, which were expressed as mean ± standard deviation and compared by ANOVA; those that did not present a normal distribution are expressed as median and interquartile range; the Mann-Whitney and Kruskal-Wallis U tests were used for comparison.

To determine the differences between the established groups, according to qualitative variables, Chi-square and Fisher's exact tests were used, as appropriate. In order to determine the LGI discriminatory power as a predictor of mortality per year, the area under receiver operating characteristic (ROC) curve was evaluated, and the optimal cut-off point was identified. Survival curves were constructed using the Kaplan-Meier method, according to the tertiles and LGI cut-off point; the survival of these groups was compared through the Log-Rank test.

To determine those factors independently associated with mortality, univariate and multivariable Cox regression was used. We included in the model those clinically significant variables or possible confounders regardless of their statistical significance, and those that in the univariate analysis presented a significance p≤0.01. A bilateral p value <0.05 was considered statistically significant.

The data was processed with SPSS version 20.0 and MedCalc version 8.2.1, both for Windows.

RESULTS

A total of 344 consecutive patients were analyzed, most of them were male (65.7%), and the median of the overall age was 68 years (interquartile range 58-76). The personal history shows that 25% had diabetes mellitus and had suffered a previous AMI, 64.2% had high blood pressure and 33.1% smoked.

The median LGI was 1.47. The patients were grouped according to the LGI tertiles corresponding to the 33rd and 66th percentiles, which were 1.207 and 1.773, respectively. When analyzing these groups, the median age was significantly higher as the LGI increased (**Table 1**). Women and diabetics presented with a significantly higher frequency in higher tertiles, while those with smoking habit predominated in the lowest. Other baseline characteristics are detailed in **table 1**.

Regarding the clinical and laboratory variables at admission according to tertiles, there were no differences in systolic and diastolic blood pressure; however, the heart rate and blood glucose, serum creatinine, blood count, neutrophil and lymphocyte count at admission were significantly higher in patients in the higher tertiles. Similarly, these groups of patients presented worse Killip-Kimbal classification (>I). No differences were found between the patients from different tertiles in terms of coronary reperfusion treatments (**Table 1**).

During mean follow-up of 278 ± 8 days, 88 deaths were recorded. The mortality rate was 25.6%, which was significantly increased by LGI tertiles (p<0.0001) and reached 55.7% in tertile 3 (**Figure 1**). The median LGI among patients who survived and died was significantly different, being higher in those who died (1.34 vs. 2.18, respectively, p<0.0001).

The area under the LGI curve was 0.715 (95% CI:

Table 1. Demographic, clinical, laboratory and treatment data.

Variables	Global (n=344)	Value of the leuko-glycemic index (LGI)			*p*
		Tertil 1 (n=114)	Tertil 2 (n=115)	Tertil 3 (n=115)	
Background					
Age (years)	68 [58-76]	65 [55-74]	69 [58-79]	71 [61-77]	0.006
Sex. female	118 (34.3)	28 (24.6)	42 (36.5)	48 (41.7)	0.020
Hypertension	221 (64.2)	65 (57.0)	79 (68.7)	77 (67.0)	0.139
Diabetes mellitus	88 (25.6)	11 (9.6)	14 (12.2)	63 (54.8)	0.000
Smoking habit	114 (33.1)	46 (40.4)	41 (35.7)	27 (23.5)	0.020
Previous myocardial infarction	86 (25)	35 (30.7)	26 (22.6)	25 (21.7)	0.225
Atrial Fibrillation	11 (3.2)	3 (2.6)	4 (3.5)	4 (3.5)	1.000
Chest Pain	96 (27.9)	37 (32.5)	28 (24.3)	31 (27.0)	0.378
Heart failure	54 (15.7)	13 (11.4)	21 (18.3)	20 (17.4)	0.300
Clinical and laboratory data on admission					
Heart rate (bpm)	78 [68.5-90]	74.5 [68-85]	79 [67-98]	84 [71-90]	0.002
Systolic BP (mmHg)	120 [110-140]	120 [110-140]	120 [110-140]	120 [100-140]	0.195
Diastolic BP (mmHg)	80 [70-85.5]	80 [70-90]	80 [70-90]	70 [60-85]	0.352
Killip-Kimball>I	141 (41.0)	31 (27.2)	48 (41.7)	62 (53.9)	0.000
Leukocytes mm^3	11.2 [10.0-12.6]	10.0 [8.6-11.0]	12.0 [10.9-13.0]	12.0 [10.4-13.2]	0.000
Neutrophils mm^3*	8.4±2.5	6.6±1.9	9.2±2.2	9.4±2.3	0.000
Lymphocytes mm^3**	2.5±0.9	2.7±1.0	2.5±0.9	2.4±0.9	0.022
Glycemia (mmol/L)	6.8 [5.7-9.0]	6.3 [5.5-8.2]	6.8 [5.7-8.5]	7.2 [5.8-12.3]	0.011
Creatinine (mmol/L)***	79.0 [65.0-103.0]	77.0 [64.0-91.1]	78.0 [64.0-103.0]	93.0 [69.0-125.0]	0.010
Coronary reperfusion treatment					
Thrombolysis	151 (43.9)	55 (48.2)	44 (38.3)	52 (45.2)	0.295
PCI	51 (14.8)	18 (15.8)	19 (16.5)	14 (12.2)	0.611

The data are presented as n (%), mean ± standard deviation, or median [interquartile range]. BP, blood pressure; LGI, leuko-glycaemic index; PCI, percutaneous coronary intervention.

* Available from 344 patients: 110 in Tertil 1 of LGI, 115 in Tertil 2 and 113 in Tertil 3.

** Available from 344 patients: 110 in Tertil 1 of LGI, 114 in Tertil 2 and 113 in Tertil 3.

*** Available from 344 patients: 100 in Tertil 1 of LGI, 107 in Tertil 2 and 106 in Tertil 3.

0.664-0.762, p<0.0001). The optimal LGI cut-value to predict mortality was 2.2; with a 50% sensitivity and an 85.9% specificity (**Figure 2**).

There were significant differences when comparing survival, which decreased according to the LGI tertiles (p<0.0001). Survival was also significantly lower (**Table 2** and **Figure 3**), in those patients with an LGI>2.2 (p<0.0001).

In the multivariate analysis, LGI>2.2 was a predictor of one-year mortality for all causes (HR 3.562, 95% CI: 2.091-6.071, p<0.0001), regardless of age, sex, Killip-Kimball>I, systolic blood pressure, serum creatinine and diabetes mellitus (**Table 3**).

DISCUSSION

In the present study, the prognostic value at 1-year LGI was evaluated in patients with ST-segment elevation AMI. Several investigations have confirmed the importance of blood count and its differential as a predictor of death and other long-term adverse

events. Núñez *et al*[6], in a prospective study of 1118 consecutive patients with acute coronary syndrome, showed, during an average 10 months follow-up, that patients with a higher white blood cell count in the first hours of admission were more likely to die. Another prospective stud-y[14] with 1037 patients, and a mean 23 months follow-up, claims that blood count and its differential is associated with a worse prognosis. An edge of this inflammatory marker has also been extensively evaluated: the neutral-lymphocyte index, with solid evidence supporting the white blood cell count and its differential as an independent marker of poor long-term prognosis[15-21].

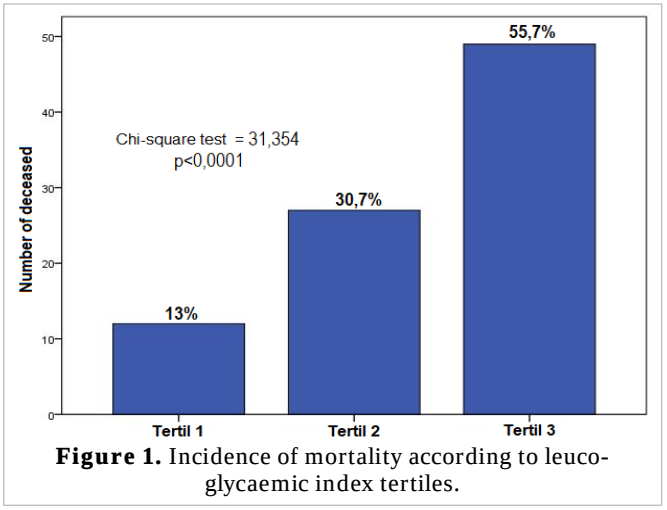

Figure 1. Incidence of mortality according to leuco-glycaemic index tertiles.

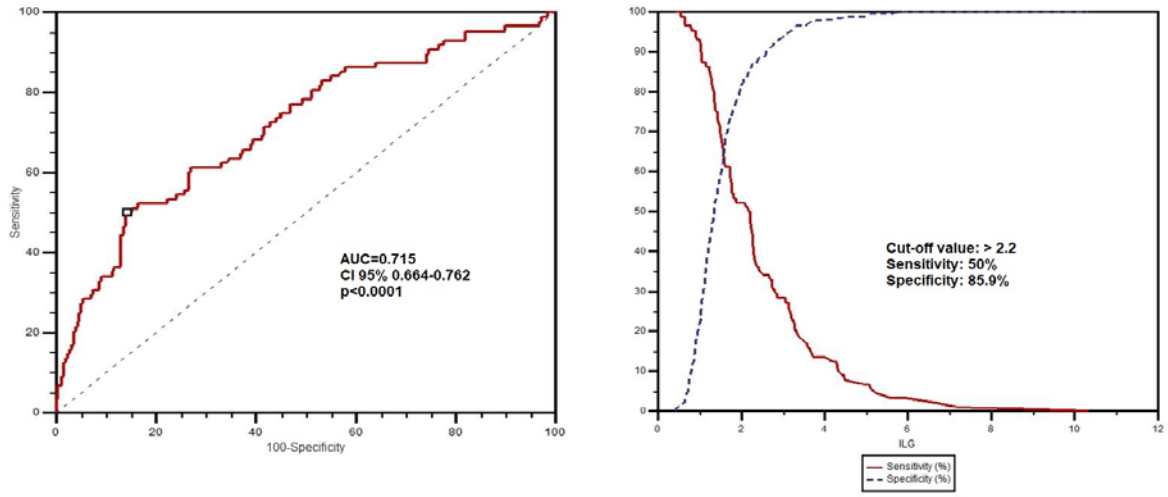

Figure 2. ROC curves showing the discrimination capacity and the optimal cut-off point of the leuco-glycaemic index to predict mortality. AUC, area under the curve; CI: confidence interval.

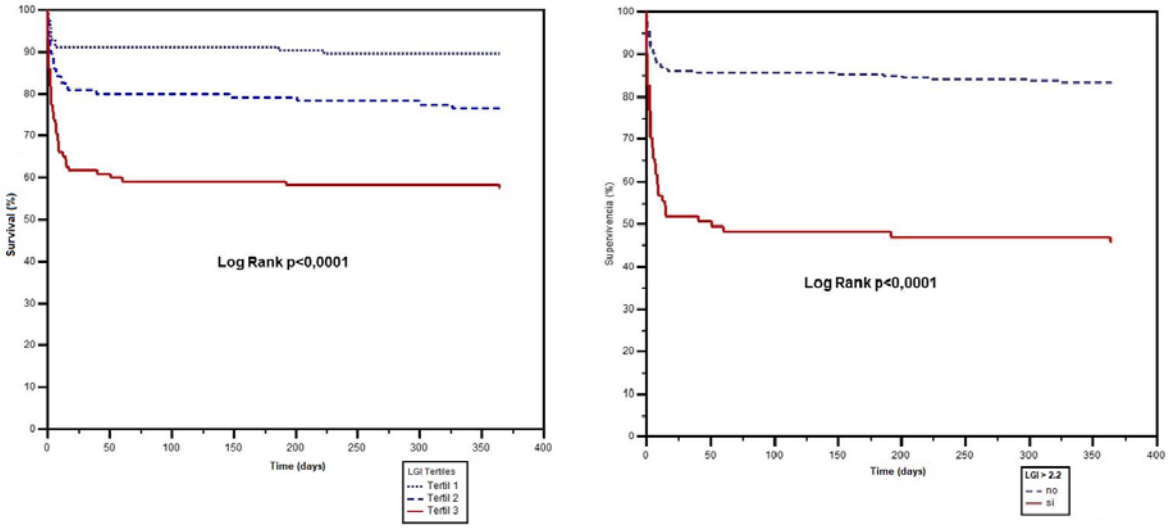

Figure 3. Kaplan-Meier survival curves of the patients studied, at 365 days, according to tertiles and leuco-glycaemic index cut-off point.

Table 2. Survival according to tertiles and LGI cut-off point.

Variable	Survival average	Typical error	CI 95%	*p* (Log Rank)
Tertil 1	330.412	9.720	311.362-349.463	
Tertil 2	288.983	13.417	262.685- 315.280	<0.0001
Tertil 3	217.313	16.363	185.242-249.384	
LGI>2.2	177.420	19.746	138.718- 216.122	<0.0001
LGI≤2.2	309.962	7.842	294.592-325.332	
Global	278 753	8.171	262.739-294.767	-

LGI, leuko-glycaemic index

Table 3. Cox, uni and multivariable proportional hazards models to evaluate the predictors of mortality per year of patients with ST-segment elevation AMI.

Variables	Univariable			Multivariable		
	p	*Hazard Ratio*	CI 95%	*p*	*Hazard Ratio*	CI 95%
LGI >2.2	<0.0001	4.187	2.752-6.369	<0.0001	3.562	2.091-6.071
Killip Kimball>I	<0.0001	5.868	3.589-9.593	<0.0001	3.502	2.083-5.888
Female sex	<0.0001	2.192	1.443-3.331	0.039	1.631	1.025-2.593
Age (years)	<0.0001	1.057	1.038-1.076	<0.0001	1.040	1.020-1.061
Creatinine (mmol/L)	<0.0001	1.005	1.003-1.006	0.002	1.004	1.001-1.006
Systolic BP (mmHg)	<0.0001	0.972	0.964-0.981	0.002	0.986	0.977-0.995
Diabetes mellitus	<0.0001	2.393	1.566-3.655	0.612	0.863	0.488-1.525

BP, blood pressure; CI, confidence interval; LGI, leuko-glycaemic index.

Many mechanisms have been proposed that explain such results. Stimulated neutrophils release free radicals, proteolytic enzymes and arachidonic acid metabolites, which increase the infarction size and lead to electric instability of the heart through endothelial damage, coagulation cascade activation, leukocyte aggregation and its deposition in microarteries[2,22]. Microparticles derived from these activated polymorphonuclear leukocytes can favor the coagulation cascade and perpetuate thrombi formation, since they can activate and favor the expression of P-selectin on the platelet[23]. In addition, elevated levels of inflammatory markers in the blood have been observed in patients with heart failure for several reasons, suggesting the strong relationship with pump failure[24].

On the other hand, glycemia as a long-term prognostic marker in patients with AMI has also been studied. A valuable study with 11324 patients shows that their admission values are a powerful predictor of mortality 20 years after having suffered an AMI[25]. Planer *et al*[26], based on the records of the multinational clinical trial HORIZONS-AMI, establish that glycemia in the first 24 hours of admission is an independent predictor of mortality at 30 days and at 3 years. Similar results were obtained in a previous study by Monteiro *et al*[27].

Hyperglycaemia is related to the size of the infarction, a greater Killip-Kimball class, low left ventricular ejection fraction, cardiogenic shock, need for resuscitation due to cardiorespiratory arrest and increased concentrations of myocardial necrosis markers[28,29]. The increase of vasoconstrictive and inflammatory factors during hyperglycemia contributes to the damage of endothelial function and increases the production of free radicals with the consequent oxidative stress[30]. In addition, there is a state of insulin resistance in which lipolysis causes free fatty acids to be released which hinders the transportation of glucose into the myocardial cell, and its oxidation generates superoxide anions[8]. It also produces an alteration in platelet metabolism

and changes in the intraplaquetic signaling mechanisms, which may contribute to the development of atherothrombotic complications[31].

The theoretical and practical evidence of the LGI components separately, as factors of worse short and long term prognosis, suggests the logical association of these in an index. Previous observations have shown that LGI constitutes a marker of poor prognosis during hospital stay. Quiroga *et al*[10] were the first to associate LGI with death and complications during hospital stay, while Benítez Díaz *et al*[13] were able to reproduce their results but with a 30-day follow-up period. Among other studies confirming the prognostic value of LGI through multivariate analysis[11,12], highlights that of Hirschson *et al*[12] when analyzing a total of 405 patients in 87 Argentinians institutions. Seoane *et al*[32] in another clinical context (postoperative period of cardiac surgery) also demonstrate −in 2743 patients− the usefulness of LGI as a predictor of poor in-hospital outcome.

However, none of the cited authors analyzes the prognostic value of LGI to predict mortality beyond 30 days; which is evaluated in the present investigation and identified as an independent predictor of mortality per year, after adjusting other variables with recognized prognostic value. In addition, this work also demonstrates for the first time that the higher LGI is a good predictor of shorter survival at 365 days in patients with AMI.

The optimal cut-off point obtained by the ROC curve to predict mortality at one year was 2.2. These results differ with the rest of the analyzed researches. Quiroga *et al*[10], León-Aliz *et al*[11], Hirchson Prado *et al*[12] and Seoane *et al*[32] found an optimal cut-off value of 1.6; 1,158; 1.00 and 2.0, respectively. These differences can be attributed mainly to the analysis period and that all assess the prognostic value of LGI in the short term, with heterogeneous samples in terms of its size and composition, and with different primary end objectives.

Study limitations

It is the experience of a single institution and the size of the sample is relatively small, although this did not prevent obtaining solid results. No data were available on the left ventricular ejection fraction, myocardial reperfusion state, or quantity and severity of the affected coronary vessels in the entire sample. In addition, the low availability of primary percutaneous coronary intervention influences the poor in-hospital survival of patients, which determines the occurrence of fewer final events after hospital discharge.

CONCLUSIONS

The results from this work support the theoretical and practical basis of the leuko-glycaemic index as a predictor of adverse events per year, in the context of acute myocardial infarction. Its simplicity, wide availability, low cost and the fact of being part of the paraclinical routine examinations performed at admission, in patients with acute coronary syndrome, further support its potential application in early risk stratification. Future larger samples multi-center studies are necessary to confirm our observations, as well as the prognostic capacity of the leucoglycaemic index in association with risk scales.

REFERENCES

1. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, *et al*. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. J Am Coll Cardiol. 2017; 70(1):1-25.
2. Ruparelia N, Chai JT, Fisher EA, Choudhury RP. Inflammatory processes in cardiovascular disease: a route to targeted therapies. Nat Rev Cardiol. 2017;14(3):133-44.
3. Eisen A, Giugliano RP, Braunwald E. Updates on acute coronary syndrome: A review. JAMA Cardiol. 2016;1(6):718-30.
4. Dimitrijevic O, Stojcevski BD, Ignjatovic S, Singh NM. Serial measurements of C-reactive protein after acute myocardial infarction in predicting one-year outcome. Int Heart J. 2006;47(6):833-42.
5. Prondzinsky R, Unverzagt S, Lemm H, Wegener NA, Schlitt A, Heinroth KM, *et al*. Interleukin-6, -7, -8 and -10 predict outcome in acute myocardial infarction complicated by cardiogenic shock. Clin Res Cardiol. 2012;101(5):375-84.
6. Núñez J, Fácila L, Llàcer À, Sanchís J, Bodí V, Vertomeu V, *et al*. Valor pronóstico del recuento leucocitario en el infarto agudo de miocardio: mortalidad a largo plazo. Rev Esp Cardiol. 2005;58(6): 631-9.
7. Guasti L, Dentali F, Castiglioni L, Maroni L, Marino F, Squizzato A, *et al*. Neutrophils and clinical outcomes in patients with acute coronary syndromes and/or cardiac revascularisation. A systematic review on more than 34,000 subjects.

Thromb Haemost. 2011;106(4):591-9.
8. Angeli F, Reboldi G, Poltronieri C, Lazzari L, Sordi M, Garofoli M, *et al*. Hyperglycemia in acute coronary syndromes: from mechanisms to prognostic implications. Ther Adv Cardiovasc Dis. 2015; 9(6):412-24.
9. Eitel I, Hintze S, de Waha S, Fuernau G, Lurz P, Desch S, *et al*. Prognostic impact of hyperglycemia in nondiabetic and diabetic patients with ST-elevation myocardial infarction: insights from contrast-enhanced magnetic resonance imaging. Circ Cardiovasc Imaging. 2012;5(6):708-18.
10. Quiroga W, Conci E, Zelaya F, Isa M, Pacheco G, Sala J, et al. Estratificación del riesgo en el infarto agudo de miocardio según el índice leucoglucémico. ¿El Killip-Kimball de laboratorio? Rev Fed Arg Cardiol. 2010;39(1):29-34.
11. León-Aliz E, Moreno-Martínez FL, Pérez-Fernández GA, Vega-Fleites LF, Rabassa-López-Calleja MA. Índice leuco-glucémico como marcador pronóstico de la evolución intrahospitalaria en pacientes con infarto agudo de miocardio con elevación del ST. Clin Investig Arterioscler. 2014; 26(4):168-75.
12. Hirschson Prado A, Higa C, Merlo P, Domine E, Blanco P, Vázquez GA, *et al*. Valor pronóstico del índice leucoglucémico en el infarto agudo de miocardio. Resultados del Registro Multicéntrico SCAR. Rev Argent Cardiol. 2014;82(6):500-5.
13. Díaz Benítez RE, Correa Morales AM, Reyes Hernández LM, Carvajal Sánchez PA, Coronado Herrera Y, González Rivera EM. Hemoglobina glucosilada e índice leucoglucémico como determinaciones pronósticas en el síndrome coronario agudo. CorSalud [Internet]. 2016 [citado 18 Jul 2018]; 8(3):153-63. Disponible en: http://www.revcorsalud.sld.cu/index.php/cors/article/view/135/321
14. Dragu R, Khoury S, Zuckerman R, Suleiman M, Mutlak D, Agmon Y, *et al*. Predictive value of white blood cell subtypes for long-term outcome following myocardial infarction. Atherosclerosis. 2008;196(1):405-12.
15. Arbel Y, Shacham Y, Ziv-Baran T, Laufer Perl M, Finkelstein A, Halkin A, *et al*. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. Can J Cardiol. 2014;30(10):1177-82.
16. Núñez J, Núñez E, Bodí V, Sanchis J, Miñana G, Mainar L, *et al*. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in ST segment elevation myocardial infarction. Am J Cardiol. 2008;101(6):747-52.
17. Cho KI, Ann SH, Singh GB, Her AY, Shin E. Combined usefulness of the platelet-to-lymphocyte ratio and the neutrophil-to-lymphocyte ratio in predicting the long-term adverse events in patients who have undergone percutaneous coronary intervention with a drug-eluting stent. PloS One [Internet]. 2015 [citado 15 Jul 2018];10(7):e0133934. Disponible en: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133934
18. Ayça B, Akin F, Celik O, Sahin I, Yildiz SS, Avci II, *et al*. Neutrophil to lymphocyte ratio is related to stent thrombosis and high mortality in patients with acute myocardial infarction. Angiology. 2015; 66(6):545-52.
19. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008;102(6):653-7.
20. Zhou D, Wan Z, Fan Y, Zhou J, Yuan Z. A combination of the neutrophil-to-lymphocyte ratio and the GRACE risk score better predicts PCI outcomes in Chinese Han patients with acute coronary syndrome. Anatol J Cardiol. 2015;15(12):995-1001.
21. Sen N, Afsar B, Ozcan F, Buyukkaya E, Isleyen A, Akcay AB, *et al*. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcome in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Atherosclerosis. 2013;228(1):203-10.
22. Kounis NG, Soufras GD, Tsigkas G, Hahalis G. White blood cell counts, leukocyte ratios, and eosinophils as inflammatory markers in patients with coronary artery disease. Clin Appl Thromb Hemost. 2015;21(2):139-43.
23. Pluskota E, Woody NM, Szpak D, Ballantyne CM, Soloviev DA, Simon DI, *et al*. Expression, activation, and function of integrin alphaMbeta2 (Mac-1) on neutrophil-derived microparticles. Blood. 2008;112(6):2327-35.
24. Arruda-Olson AM, Reeder GS, Bell MR, Weston SA, Roger VL. Neutrophilia predicts death and heart failure after myocardial infarction: a community-based study. Circ Cardiovasc Qual Outcomes. 2009;2(6):656-62.
25. Deckers JW, van Domburg RT, Akkerhuis M, Nauta ST. Relation of admission glucose levels, short-

and long-term (20-year) mortality after acute myocardial infarction. Am J Cardiol. 2013;112(9): 1306-10.
26. Planer D, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Xu K, *et al*. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. Int J Cardiol. 2013;167(6):2572-9.
27. Monteiro S, Monteiro P, Gonçalves F, Freitas M, Providência LA. Hyperglycaemia at admission in acute coronary syndrome patients: prognostic value in diabetics and non-diabetics. Eur J Cardiovasc Prev Rehabil. 2010;17(2):155-9.
28. Ladeira RT, Baracioli LM, Faulin TE, Abdalla DS, Seydell TM, Maranhão RC, *et al*. Unrecognized diabetes and myocardial necrosis: predictors of hyperglycemia in myocardial infarction. Arq Bras Cardiol. 2013;100(5):404-11.
29. Naber CK, Mehta RH, Jünger C, Zeymer U, Wienbergen H, Sabin GV, *et al*. Impact of admission blood glucose on outcomes of nondiabetic patients with acute ST-elevation myocardial infarction (from the German Acute Coronary Syndromes [ACOS] Registry). Am J Cardiol. 2009; 103(5):583-7.
30. Koraćević G, Vasiljević S, Velicković-Radovanović R, Sakac D, Obradović S, Damjanović M, *et al*. Stress hyperglycemia in acute myocardial infarction. Vojnosanit Pregl. 2014;71(9):858-69.
31. Puig Domingo M. Función plaquetaria e hiperglucemia en el síndrome coronario. Rev Esp Cardiol. 2014;67(1):3-5.
32. Seoane LA, Korolov Y, Vrancic M, Camporrotondo M, Piccinini F, Hirschson Prado A, *et al*. Valor pronóstico del índice leucoglucémico en el postoperatorio de cirugía cardíaca. Cir Cardiov. 2017; 24(6):335-9.