

# Neutrophil-lymphocyte ratio for the diagnosis of type 4a myocardial infarction

## Índice neutrófilo-linfocitario en el diagnóstico de infarto de miocardio tipo 4a

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### ABSTRACT

**Introduction.** Periprocedural type 4a myocardial infarction is among the complications associated with percutaneous coronary interventions. The important role played by inflammation in cardiovascular disease is well-known, and a better expression of this inflammatory state is the neutrophil-lymphocyte ratio.

**Objective.** To assess the association between the neutrophil-lymphocyte ratio and the appearance of type 4a myocardial infarction and the potential diagnostic value of this biological marker.

**Methodology.** Applied, descriptive-correlational, and prospective study. The neutrophil-lymphocyte ratio was obtained six hours after coronary intervention at the "Hermanos Ameijeiras" Hospital, Havana, Cuba, between November 2018 and January 2020.

**Results.** A total of 184 patients were studied, 25 of whom developed type 4a infarction. In patients with heart attack, the ratio increased after the procedure [ $4.26 \pm 0.95$ ; (3.87-4.65)] vs [ $3.19 \pm 0.86$ ; (2.83-3.54)]. Ratios  $>2.63$  were associated with the diagnosis of the complication, with an area under the ROC curve for diagnosis of 0.932 (95%CI: 0.868-0.995;  $p < 0.001$ ).

**Conclusions.** The neutrophil-lymphocyte ratio has high sensitivity, high specificity, and high positive and negative predictive values in the diagnosis of type 4a myocardial infarction.

**Keywords:** neutrophil-lymphocyte ratio, periprocedural type 4a myocardial infarction.

### RESUMEN

**Introducción.** Dentro de las complicaciones relacionadas con el intervencionismo coronario percutáneo se encuentra el infarto del miocardio periprocedimiento tipo 4a. Se conoce el importante papel que juega la inflamación en las enfermedades cardiovasculares, y una mejor expresión de este estado inflamatorio es el índice neutrófilo-linfocitario (INL).

**Objetivo.** Evaluar la asociación entre el índice neutrófilo-linfocitario y la aparición del infarto del miocardio tipo 4a así como el potencial valor diagnóstico de este marcador biológico.

**Metodología.** Investigación aplicada, descriptiva-correlacional y prospectiva. En el Hospital Hermanos Ameijeiras, La Habana, Cuba, entre noviembre de 2018 y enero de 2020, se determinó el INL a las seis horas de la intervención coronaria.

**Resultados.** Se estudiaron 184 pacientes, 25 de estos desarrollaron infarto tipo 4a. En los pacientes con infarto se incrementó el índice después del proceder [ $4,26 \pm 0,95$ ; (3,87-4,65)] vs [ $3,19 \pm 0,86$  (2,83-3,54)]. Un índice mayor de 2,63 se asoció al diagnóstico de la complicación, con un área bajo la curva ROC para el diagnóstico de 0,932 (IC95%: 0,868-0,995;  $p < 0,001$ ).

**Conclusiones.** El índice neutrófilo-linfocitario tiene alta sensibilidad, alta especificidad y altos valores predictivos positivos y negativos en el diagnóstico de infarto del miocardio tipo 4a.

**Palabras claves:** índice neutrófilo-linfocitario, infarto de miocardio periprocedimiento tipo 4a.

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## INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality worldwide<sup>1</sup>. Ischemic heart disease ranks #1 as the leading cause of death and disability<sup>2</sup>. In Europe, this condition represents 19% of deaths in males and 20% in women<sup>3</sup>; in the United States an acute myocardial infarction is reported every 40 seconds with a mean age of 65 years for males and 72 years for women<sup>4</sup>. In Cuba, cardiovascular disease is the leading cause of death. Back in 2018, ischemic heart disease killed 16,260 people (63.31%) and is the most common single cause of death among Cubans<sup>5</sup>. In order to fight it several advances have been made by developing the main therapeutic tools available today: optimal medical treatment with drugs that starts by preventing cardiovascular risk factors and training the population to change these factors at all levels of healthcare; rehab; coronary revascularization surgery; and percutaneous coronary intervention (PCI)<sup>6</sup>.

## HISTORY

Percutaneous coronary intervention is one of the most widely developed areas in contemporary cardiology<sup>7</sup>. Several advances made in the techniques and materials used have gradually brought PCI to more and more complex settings such as bifurcation lesions, thin vessels, calcified lesions, angulated lesions, left main coronary artery lesions, chronic total coronary occlusions, and other<sup>8,9</sup>. Periprocedural type 4a myocardial infarction (type 4a MI) is a complication associated with PCI. One of the diagnostic criteria for type 4a MI is the release of proteins from myocardial cells in a certain amount<sup>10,11</sup>. In cardiology the definition of this complication is controversial since there is no agreement on the diagnostic criteria and, most important of all, the availability and accessibility of validated markers is scarce<sup>10</sup>. The rate of type 4a MI reported is highly variable going from 2.6% all the way up to 30%<sup>12,13</sup> and has implications in the prognosis of patients, which is why its detection and stratification is essential to guide treatment<sup>12</sup>.

The role of inflammation in cardiovascular disease is important as well as the role it plays in atherosclerotic plaque progression and destabilization, the leading cause of coronary artery disease (CAD)<sup>14-16</sup>. The CANTOS clinical trial showed how interleukin-1 beta inhibition lowers the C-reactive protein levels and the occurrence of cardiovascular events beyond the 30 day-mark in patients with acute coronary syndrome<sup>17</sup>. White blood cells and their different subtypes are among the various inflammatory markers that exist; inflammatory pro-

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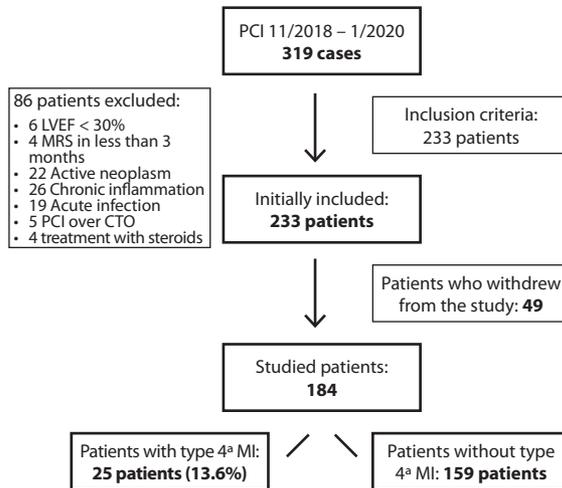


Figure 1. Study flow chart.

cess raises the levels of neutrophils, reduces the levels of lymphocytes, and is associated with more cardiovascular risk factors<sup>18,19</sup>. Neutrophils secrete inflammatory mediators like the proteolytic enzyme elastase that degrades the vascular basement membrane and causes endothelial damage<sup>20</sup>. On the other hand, lymphocytes regulate the inflammatory response and have inhibitory effects on atherosclerosis<sup>21</sup>.

A better expression of this inflammatory state is the neutrophil-lymphocyte ratio (NLR). The NLR is easy to obtain, cost-effective, commonly used, reproducible, and widely available in all centers in our country; increases of the NLR are associated with adverse cardiovascular events, mortality included, in patients with myocardial infarction (MI) and adverse clinical results in patients treated with elective coronary revascularization<sup>19,22</sup>.

Type 4a MI as a complication of PCI is associated with a torpid course of the disease in this subgroup of patients. A possible correlation between the NLR and type 4a MI, with high sensitivity and specificity, and high predictive values would place the NLR as a cheaper and more available diagnostic marker of type 4a MI to benefit patients who undergo this procedure.

## OBJECTIVE

To assess the correlation between the NLR and the appearance of type 4a MI and the diagnostic value of this biological marker.

## PARTICIPANTS AND METHOD

Applied, descriptive-correlational, and prospective study of a total of 148 consecutive patients treated at the cath lab of the Hospital “Hermanos Ameijeiras” in Havana, Cuba, between November 2018 and January 2020. A total of 233 of 319 patients treated with PCI during this period were initially included. Forty-nine of these patients were eventually excluded due to incomplete data in the clinical history (Figure 1).

### Percutaneous coronary intervention and drugs

Both the PCI technique and the decision on the type of stent to be used were left to the operator’s criterion. Unfractionated heparin was used in all the patients during the procedure to achieve activated clotting times >250 seconds during the procedure; the patients were on dual antiplatelet therapy.

TABLE 1. Características sociodemográficas y antecedentes personales de la población estudiada.

Social and demographic characteristics and past medical history	Type 4a MI			P
	Total (n=184) n (%)	Yes (n=25) n (%)	No (n=159) n (%)	
Age (mean ± SD)	61,4±14,2	57,6±12,2	62,0±14,4	0,097 <sup>a</sup>
Sex				
Male	123 (66,8)	16 (64,0)	107 (67,3)	0,923 <sup>b</sup>
Female	61 (33,2)	9 (36,0)	52 (32,7)	
Personal past medical history				
AHT	129 (70,1)	16 (64,0)	113 (71,1)	0,629 <sup>b</sup>
DM	66 (35,9)	14 (56,0)	52 (32,7)	0,042 <sup>b</sup>
CKD	24 (13,0)	7 (28,0)	17 (10,7)	0,026 <sup>c</sup>
Previous MI	93 (50,5)	13 (52,0)	80 (50,3)	1,000 <sup>b</sup>
Previous revascularization				
No	142 (77,2)	17 (68,0)	125 (78,6)	d
PCI	37 (20,1)	4 (16,0)	33 (20,89)	
MRS	4 (2,2)	4 (16,0)	0 (0,0)	
Hybrid	1 (0,5)	1 (0,6)	0 (0,0)	
Smoking				
Does not smoke	76 (41,3)	7 (28,0)	69 (43,4)	0,215 <sup>e</sup>
Smoker	70 (38,0)	10 (40,0)	60 (37,7)	
Former smoker	38 (20,7)	87 (32,0)	30 (18,9)	

AHT, arterial hypertension; CKD, chronic kidney disease; DM, diabetes mellitus; MI, myocardial infarction; MRS, myocardial revascularization surgery; PCI, percutaneous coronary intervention; SD, standard deviation; a, Mann-Whitney U test; b, chi-square test with correction; c, Fisher’s exact test; d, not valid chi-square test since 50.0% of the anticipated frequencies were < 5; e, chi-square test ( $\chi^2$ )

## Neutrophil-lymphocyte ratio

The NLR was defined as the ratio between the absolute value of neutrophils and the absolute value of lymphocytes. It was obtained before the PCI (within the previous 7 days) and 6 hours after the PCI. The leukogram was performed using the Pentra-DX NEXUS analyzer. This is a fully automatic hematology analyzer for the in-vitro diagnosis of whole blood samples anticoagulated with EDTA at 10% capable of testing 120 samples an hour. The following parameters were analyzed:

- Lymphocytes: [LYN], expressed as absolute value (#).
- Neutrophils: [NEU], expressed as absolute value (#).

## Ethical considerations

This clinical study was conducted according to the last review of the Declaration of Helsinki. All the patients involved in the study were informed of the characteristics of the study and procedures used and gave their written informed consent prior to their participation.

## Techniques used for statistical analysis

In order to identify the factors associated with the appearance of type 4a MI, the logistic regression function that models the probability of suffering this disease was estimated.

The model was adjusted with variables based on scientific evidence and on the researchers’ experience in such a way that the variables would not be correlated and the sizes of the samples within each group allowed the most accurate estimate possible of the parameters in the logistic regression equation. The point estimates of odds ratios (OR) and 95% confidence intervals (95%CI) were calculated for every variable; Hosmer-Lemeshow goodness-of-fit statistical test was used to assess the quality of adjustment of the logistic regression model.

## RESULTS

The social, demographic, clinical, anatomical, and procedural characteristics are all shown on Tables 1, 2, and 3.

**TABLE 2.** Characteristics of the patients based on clinical and anatomical variables.

Clinical variables	Type 4a MI <sup>a</sup>			p
	Total (n=184) n (%)	Si (n=25) n (%)	No (n=159) n (%)	
LVEF 30% - 50%	63 (34,2)	15 (64,0)	48 (31,4)	<b>0,003<sup>a</sup></b>
LVEF mayor 50 %	121 (65,8)	10 (40,0)	111 (69,8)	<b>0,097<sup>a</sup></b>
Diagnosis				
CSAE	72 (39,1)	11 (44,0)	61 (38,4)	<b>0,749<sup>b</sup></b>
NSTEACS	99 (53,8)	13 (52,0)	86 (54,1)	
STEACS	13 (7,1)	1 (4,0)	12 (7,5)	
Anatomical variables				
Multivessel CAD	89 (48,4)	15 (60,0)	74 (46,5)	<b>0,300<sup>c</sup></b>
SYNTAX (median/IQR)	11,0/15,0	21,0/15,0	11,0/12,0	<b>&lt;0,001<sup>c</sup></b>
Multi-arterial PCI	52 (28,3)	14 (56,0)	38 (23,9)	<b>0,002<sup>c</sup></b>
Type of lesion treated				
Type A	121 (65,82)	10 (40,0)	111 (69,8)	<b>d</b>
Type B1	16 (8,7)	7 (28,0)	9 (5,7)	
Type B2	46 (25,0)	7 (28,0)	39 (24,5)	
Type C	1 (0,5)	1 (4,0)	0 (0,0)	
Thrombus	5 (2,7)	4 (16,0)	1 (0,6)	<b>0,001<sup>e</sup></b>
Severe calcification	43 (23,4)	5 (20,0)	38 (23,9)	<b>0,862<sup>a</sup></b>
Bifurcation lesion	85 (46,2)	17 (68,0)	68 (42,8)	<b>0,033<sup>a</sup></b>
Bifurcverd	54 (29,3)	16 (64,0)	38 (23,9)	<b>&lt;0,001<sup>a</sup></b>

CAD, coronary artery disease; CSAE, chronic stable angina provoked by exertion; IQR, interquartile range; LVEF, left ventricular ejection fraction; NSTEACS, non-ST-elevation acute coronary syndrome; STEACS, ST-elevation acute coronary syndrome; SYNTAX, score according to the SYNTAX scale; a, chi-square test with correction; b, chi-square test; c, Mann-Whitney U test; d, chi-square test not valid since 37.5% of the anticipated frequencies are <5; e, Fisher's exact test.

There are significant differences ( $p<.001$ ) between the absolute neutrophil count and absolute lymphocyte count and the NLR before and after the procedure. The values of these absolute counts and the NLR increased after the procedure was performed on the patients (**Table 4**).

Between the 2 groups of patients (with type 4a MI and without infarction), except for the absolute neutrophil count before the procedure ( $5.46\pm 1.21$  vs.  $5.53\pm 1.15$ ;  $p=.599$ ), there were very significant differences ( $p<.001$ ) in the absolute neutrophil count after the procedure ( $8.26\pm 0.99$  vs.  $6.32\pm 0.66$ ), the absolute lymphocyte count before ( $1.68\pm 0.48$  vs.  $2.26\pm 0.40$ ) and after ( $2.03\pm 0.47$  vs.  $2.62\pm 0.31$ ) the procedure, and the NLR before ( $3.19\pm 0.86$  vs.  $2.51\pm 0.50$ ) and after the procedure ( $4.26\pm 0.95$  vs.  $2.40\pm 0.28$ ). Both in the group of patients with type 4a MI and in the group of patients without infarction, there were very significant differences ( $p<.001$ ) between the absolute neutrophil count, the absolute lymphocyte count and NLR before and after the procedure. These results are shown on **Chart 1**.

The area under the ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the procedure was 0.932 (95%CI: 0.868-0.995;  $p<.001$ ) (**Chart 2**).

For the NLR cut-off value  $\geq 2.63$ , sensitivity was 84.0% (95%CI: 67.6-100%), meaning that it can detect 84.0% of the patients with an actual diagnosis of type 4a MI. Specificity was 74.2% (95%CI, 67.1-81.3%), meaning that it can identify 74.2% of the patients without infarction (**Table 5**). The PPV was 33.9% (21.3%-46.5%) meaning that the percentage of patients with type 4a MI within those with NLR  $\geq 2.63$  was 33.9%. The NPV was 96.7% (95%CI: 93.2%-100%), meaning that the percentage of patients without type 4a MI within those with NLR  $<2.63$  was 96.7% (**Table 5**). The VR+ was 3.3 (95%CI: 2.4-4.5) and the VR- was 0.2 (95%CI: 0.1-0.5), meaning that NLRs  $\geq 2.63$  are nearly 3 times more likely in patients with type 4a MI compared to patients without type 4a MI and NLRs  $<2.63$  are 5 times more likely (1/0.2)

**TABLE 3.** Characteristics of the patients based on their hemodynamic variables.

Hemodynamic variables	Type 4a MI			p
	Total (n=184) n (%)	Si (n=25) n (%)	No (n=159) n (%)	
Simple bifurcation technique	81 (56,0)	13 (52,0)	68 (42,8)	<b>0,517<sup>a</sup></b>
Complex bifurcation technique	4 (2,2)	4 (16,0)	0 (0,0)	<b>&lt;0,001<sup>b</sup></b>
Type of complex technique				
No	180 (97,8)	21 (84,0)	159 (100)	<b>c</b>
Culotte	3 (1,1)	2 (8,0)	1 (0,6)	
TAP	1 (0,5)	1 (4,0)	0 (0,0)	
DK-crush	2 (0,5)	1 (4,0)	1 (0,6)	
Double kissing balloon	26 (14,1)	6 (24,0)	20 (12,6)	<b>&lt;0,001<sup>b</sup></b>
Type of stent				
Drug-eluting	136 (73,9)	18 (72,0)	118 (74,4)	<b>1,000<sup>a</sup></b>
Conventional	48 (26,1)	3 (14,3)	45 (27,6)	
# Implanted stents (median/IQR)	1,5/2,0	2,0/2,0	1,0/1,0	<b>0,006<sup>d</sup></b>
Total length of stented segment	23,0/16,0	28,0/12,0	23,0/10,0	<b>0,001<sup>d</sup></b>
Diameter of the stent	3,0/1,0	3,0/1,0	3,0/1,0	<b>0,273<sup>d</sup></b>
Angiographic success	159 (86,4)	9 (36,0)	150 (94,3)	<b>0,081<sup>b</sup></b>

DK-crush, double kissing crush technique; IQR, interquartile range; TAP, stenting and small protrusion technique; a, chi-square test with correction; b, Fisher's exact test; c, chi-square test not valid since 75.0% of the anticipated frequencies are <5; d, Mann-Whitney U test.

**TABLE 4.** Descriptive statistics of the absolute neutrophil count, absolute lymphocyte count, and NLR before and after the procedure.

Statistics	ANC pre	ANC post	ALC pre	ALC post	NLR pre	NLR post
Median $\pm$ SD	5,5 $\pm$ 1,2	6,6 $\pm$ 1,0	2,2 $\pm$ 0,5	2,5 $\pm$ 0,4	2,6 $\pm$ 0,6	2,7 $\pm$ 0,8
95%CI	5,4-5,7	6,4-6,7	2,1-2,2	2,4-2,6	2,5-2,7	2,5-2,8
Minimum	2,0	4,1	1,1	1,1	1,5	1,0
Maximum	8,0	10,2	3,0	3,5	4,9	6,2
$p^a$	<b>&lt;0,001</b>		<b>&lt;0,001</b>		<b>0,060</b>	

95%CI, 95% confidence interval; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; NLR, neutrophil-lymphocyte ratio; SD, standard deviation; a, Wilcoxon sign-rank test.

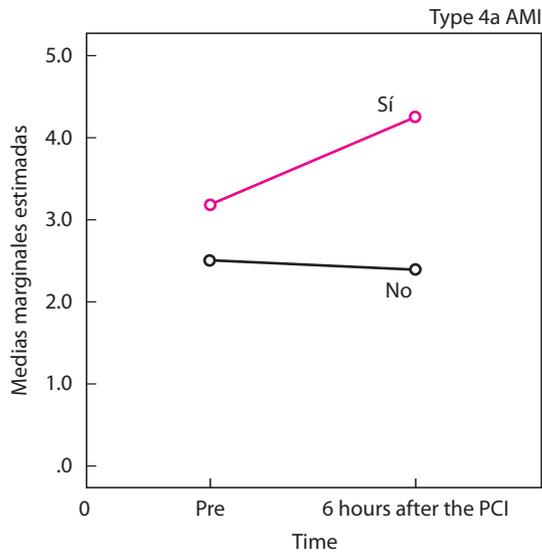
in patients without type 4a MI compared to patients with this disease (**Table 5**).

The variables that play an independent role in the presence of type 4a infarction were the past medical history of CKD, previous revascularization, and the NLR obtained 6 hours after the procedure.

The OR for CKD was 10.515 (95%CI: 1.123-98.471), the OR (chance or opportunity) of having type 4a MI is nearly 10 times higher in patients with a past medical history of CKD compared to patients without this disease. The OR of previous revascularization was 4.117 (95%CI: 1.115-15.199), the OR of having type 4a MI is nearly 4 times higher in patients with previous revascularization compared to patients without it. The OR for NLRsobtained 6 hours after the procedure was 81.395 (11.933-555.210). Finally, the OR of having type 4a MI increases parallel to the increase of such variable (**Table 6**).

## DISCUSSION

The fourth universal definition of myocardial infarction describes MI as related to the PCI with higher concentrations in the markers of myocardial damage above the 99th percentile of the upper reference limit within the first few hours after the intervention. To this day, the most highly specific and sensi-



**Chart 1.** Means of NLR before and after the procedure based on the presence of type 4a MI.

**TABLE 5.** Indicators of the validity of the NLR 6 hours after the procedure for the diagnosis of type 4a MI.

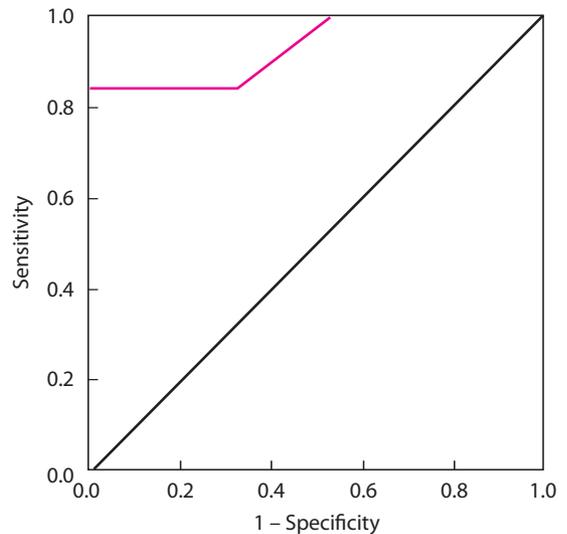
Indicators	NLR 6 hours after the procedure ( $\geq 2.63$ )	
	Point estimates (%)	95%CI
Sensitivity	84,0	67,6-100
Specificity	74,2	67,1-81,3
PPV <sup>a</sup>	33,9	21,3-46,5
NPV <sup>a</sup>	96,7	93,2-100
LR+	3,3	2,4-4,5
LR-	0,2	0,1-0,5

95%CI, 95% confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NLR, neutrophil-lymphocyte ratio; NPV, negative predictive value; PPV, positive predictive value; a, prevalence of type 4a MI=13.6%, 95%CI: 8.4%-18.8%.

ve validated markers are cardiac troponins T and I, the creatine kinase MB isoenzyme (CK-MB)—the most specific isoform of the heart muscle—plus clinical evidence or images of ischemia or angiographic alterations<sup>11</sup>. In this study, the frequency of type 4a MIs is similar to that reported in the medical literature<sup>13,14,23</sup>.

The sudden decrease of blood flow to a myocardial territory during the PCI can be due to several causes like loss of blood flow or slow flow to a secondary branch, distal embolization of thrombus or material from the atherosclerotic plaque, the transient occlusion of a vessel, no-reflow or slow flow in the main vessel, and residual dissection, among others. This coronary flow disorder is associated with metabolic changes accompanied by an acute inflammatory state both in the myocardium damaged and in the location of the coronary anatomy damaged. Myocardial necrosis induces the generation and activation of free radicals, starts the cytokine storm, and releases the tumor necrosis factor- $\alpha$ <sup>18</sup>.

The role of inflammation in the pathophysiology of growth and instability of atherosclerotic coronary artery disease has been established by scientific evidence<sup>24,25</sup>. The inflammatory response is associated with a prothrombotic state that increases fibrinogen levels, coagulation factors, and platelet reactivity<sup>26</sup>. The results of this study show that the clinical, anatomical, and procedural elements involved with a greater inflammatory state are significantly associated with the presence of type 4a MI.



**Chart 2.** ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the procedure.

**TABLE 6.** Results of multivariate analysis for the presence of type 4a MI.

Variables	OR	95%CI	P
CKD	10,515	1,123-98,471	<b>0,039</b>
DM	1,032	0,126-8,419	0,977
Previous revascularization	4,117	1,115-15,199	<b>0,034</b>
NLR 6 hours after the procedure	81,395	11,933-555,210	<b>&lt;0,001</b>

95%CI, 95% confidence interval; CKD, chronic kidney disease; DM, diabetes mellitus; NLR, neutrophil-lymphocyte ratio; OR, odds ratio.

Diabetes mellitus, chronic kidney disease (CKD), and left ventricular systolic dysfunction establish a systemic inflammatory state. Diabetic macroangiopathy causes more vulnerable and extensive coronary lesions in diffusely diseased coronary vessels, anatomical conditions that increase the risk of having a type 4a MI<sup>27</sup> and other complications during the PCI; CKD and left ventricular systolic dysfunction are associated with inflammation and can be the cause of extensive and complex coronary disease<sup>28-30</sup>. Inflammation increases the vulnerability of coronary plaque followed by risk of rupture and dissection during the PCI<sup>28</sup>; Kurtul A et al.<sup>31</sup> showed that an inflammatory state before the primary PCI, expressed as a high NLR, is associated with no-reflow.

In this study, the anatomical characteristics of coronary arteries indicative of a higher atherosclerotic burden like moderately high scores, presence of thrombus, true bifurcation lesions, and the complex double coronary bifurcation stenting technique were associated with the presence of type 4a MI. Atherosclerotic burden is associated with the inflammatory state; in a former study, the author found that higher NLRs prior to an invasive coronary angiography was associated with significantly higher SYNTAX scores<sup>32</sup>. The presence of thrombus increases the risk of distal embolization, severe spasm, and no-reflow or slow reflow during the procedure and is associated with higher NLRs<sup>33</sup>.

The NLR is a biomarker that expresses the emergent systemic and coronary inflammatory state. Percutaneous coronary interventions cause inflammation after the cannulation of coronary ostia, the injection of iodinated contrast, the insertion and expansion of intracoronary devices, among others. The NLR as an expression of inflammation increases after the in-

vative procedure<sup>34,35</sup>. No significant increase was seen in this series, but an absolute neutrophil count increase was reported. The biomarkers established for the diagnosis of type 4a MI are the TnT and the CK-MB<sup>11,12</sup> and they express cardiac inflammation. There is not enough evidence on the association between the NLR and the presence of myocardial damage during the PCI. In this study, 6 hours after the PCI, the NLR was >2.63 and it was associated with the occurrence of periprocedural infarction. With an acceptable sensitivity and specificity, and a high NPV, the area under the ROC curve for the diagnosis of type 4a MI based on the NLR obtained 6 hours after the PCI is rather good since it is >0.8. Also, based on the 95%CI, it could be up to 0.995. The study conducted by Verdoia et al. reported similar results in patients treated with a PCI in a stable clinical context where NLRs  $\geq 3$  were associated with the occurrence of type 4a MI.

On the utility of the NLR for the diagnosis of type 4a MI, the values of estimated sensitivity and specificity in this series can be considered good because they are high. Actually, they are close to 100%. However, the PPV is not good because predictive values are influenced by the prevalence of the disease they

are trying to diagnose. That is why the NPV is high, because the lower the prevalence of the disease the higher the NPV and the lower the PPV.

Likelihood ratios are also accepted. It has been considered that diagnostic means (in this case the NLR) have good diagnostic efficacy with LR+ as high as they can be and LR- as close to 0 as possible.

In the multivariate analysis, CKD, previous revascularization, and the NLR obtained 6 hours after the procedure were independently associated with type 4a MI. This result is telling us that the NLR is an inflammatory biomarker that can be useful for the risk stratification of patients treated with PCI to predict and diagnose type 4a MI.

## CONCLUSIONS

The neutrophil-lymphocyte ratio obtained 6 hours after a percutaneous coronary intervention is significantly higher compared to the baseline NLR of patients with type 4a MI. This ratio has high sensitivity, high specificity, and high positive and negative predictive values for the diagnosis of type 4a MI

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