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# Neutrophile-Lymphocyte Index in Patients with Peripheral Arterial Disease

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**Abstract- Introduction:** It has been demonstrated that inflammatory processes play a leading role in many chronic diseases and that they are producers of endothelial dysfunction that cause the symptoms and signs of these diseases, determining their levels of morbidity and mortality in most of them. Its early detection and assessment will allow us to adequately control it. The Neutrophil-Lymphocyte Index has demonstrated its value as a prognostic factor for inflammatory processes, which is why it has been applied in patients with peripheral arterial disease (PAD).

**Material and method:** The sample was made up of all patients with PAD and underwent surgery, determining the N / L index levels before and after surgery in 24 hours, 15 days, 30 days, 60 days, 90 days, and 365 days.

**Keywords:** index, neutrophils, lymphocytes, risk, morbidity and mortality.

**GJMR-I Classification:** NLMC Code: WG 510



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# Neutrophile-Lymphocyte Index in Patients with Peripheral Arterial Disease

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**Material and method:** The sample was made up of all patients with PAD and underwent surgery, determining the N / L index levels before and after surgery in 24 hours, 15 days, 30 days, 60 days, 90 days, and 365 days.

**Results:** N / L index, in pre-operative low risk 36.7%, intermediate 37.7% and high 25.4%, surgery performed low risk 54.9%, intermediate 28.4% and high to 16.6% (INL > 3) at 24 hours 2 acute thromboses, 1 at 15 and 60 days, with 2 prosthesis sepsis at 90 days. INL reached 5 or more, at 24 hours 2 deaths, 2 thromboses, 90 days 2 amputees and more than 365 days, 1 acute occlusion, 1 amputee. The most frequent complication is thrombosis of the revascularization procedure. Mortality 0.98 with two deaths in the first 24 hours of the procedure where the IN / L was always above 5. A cumulative patency of 89.7% was achieved.

**Conclusion:** Prognostic value of IN / L is extremely useful in the prevention of amputations, morbidity and mortality, and cumulative patency

**Keywords:** index, neutrophils, lymphocytes, risk, morbidity and mortality.

## 1. INTRODUCTION

Atherosclerosis (AEO) is the main etiology in arterial diseases with production of tissue ischemia, necrosis and therefore loss of limbs or life if they are not treated properly, so its prevention plays a

leading role in its treatment, monitoring and control <sup>(1-2)</sup>. The neutrophil / lymphocyte ratio (INL) has been proposed as a predictor of vascular risk and indicator of atherosclerosis, therefore, it has been suggested that the management of this index is an excellent marker in the prediction of mortality and cumulative patency in revascularizations for peripheral arterial disease <sup>(3-7)</sup>. Annually, cardiovascular diseases (CVD) where arteriosclerosis plays its main etiological role, cause about 4 million deaths in Europe, which accounts for 47% of all deaths and 40% in the European Union. Peripheral vascular diseases, also of the same etiology, play a fundamental role in the figures for mortality and expenses in medical care. Very similar statistics on morbidity and mortality reflect the studies in the United States, even exceeding them on many occasions. <sup>(1)</sup> The multisystemic nature of AEO makes both coronary artery disease, as well as vascular-cerebral and peripheral arterial disease, present with high rates in many developed or developing countries. The cost of CVD in Europe is 196,000 million euros per year <sup>(1-2)</sup>. The high prevalence of primary risk factors, vulnerable or not, helps the development of diseases caused by atherosclerosis. This places its detection and control in a very high priority position. The World Health Organization considers that 75% of deaths from these diseases could be prevented with appropriate changes in lifestyle and modification of risk factors. Consequently, the early detection of patients with cardiovascular risk constitutes an objective to prioritize <sup>(2)</sup>. The determination of the systemic inflammatory state is emerging as a new prognostic marker, mainly in the field of oncology, cardiovascular diseases, vascular brains and peripheral arteries <sup>(3-5)</sup>. The neutrophil / lymphocyte index has been established as a potential marker of systemic endothelial dysfunction, very inexpensive, non-invasive, repeatable, very accessible, extremely fast and independent of all other known biological factors or not, especially in asymptomatic patients <sup>(3-6)</sup>. Among the pathogenic mechanisms described in atherosclerosis, endothelial dysfunction stands out both at the microvascular level with decreased nitric oxide, increased Von Willebrand factor, vascular endothelial growth factor (VEGF), dimethylarginine asymmetric, as well as the macrovascular given by vasodilation. This damage is sometimes explained by inflammation of the

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endothelium of the microvasculature, which favors the accumulation of lipids and the progress of atherosclerosis. This neutrophil / lymphocyte index (INL) is defined as the absolute neutrophil count divided by the lymphocyte count and allows us to demonstrate the balance that exists between the neutrophil active component of the systemic inflammatory response and the lymphocytes considered the regulatory and protective component.

It is the reason why an elevated INL is representative of a degree of inflammation exceeded <sup>(5-11)</sup> Unlike other markers, this does not require specific quantification in its analysis, therefore it constitutes a very efficient, low-cost, easy-to-obtain and very useful evaluation element for patients who are going to undergo cardiac surgery and vascular <sup>(8-11)</sup>.

## II. SCIENTIFIC PROBLEM

The need to establish adequate behaviors in the prediction of morbidity, mortality and cumulative patency in patients undergoing revascularization surgery supports the performance of this study because, unlike other markers, it is very efficient, inexpensive, easy to obtain and very useful, for patients who are going to undergo both cardiac and vascular surgery

## III. OBJECTIVES

Describe the clinical evolution of patients undergoing revascularization due to peripheral arterial disease and, through the neutrophil-lymphocyte index (INL), establish a prognostic marker of cumulative patency, according to the level of risk and multisystematization of the arteriosclerotic disease.

## IV. METHODOLOGY

A longitudinal descriptive study was carried out in patients undergoing revascularization due to peripheral arterial disease, treated at the Ernesto Che Guevara Cardiocentro in Santa Clara, CUBA in the period July 2017 to July 2020, with the aim of specifying the evolution of these patients through the Neutrophil-lymphocyte index (INL) as a prognostic marker of the disease through cumulative patency. The study population was made up of all the patients who underwent revascularization interventions for peripheral arterial disease, attended by the Cardiocenter Vascular Surgery Service in the indicated period and who met the inclusion criteria, agreeing to participate in study and attend all consultations according to the established schedule, to monitor the neutrophil-lymphocyte index As exit criteria, patients who died during the study period or those who did not want to remain in it were taken into account. The sample was made up of 204 patients. All the patients included in this study underwent hematological tests within the preoperative period and calculations of the neutrophil and lymphocyte numbers, before the intervention, 24 hours after the operation, at 15 days, at one month, at two and at three months and in cases of more than a year after the operation, they attended the vascular surgery outpatient clinic. The degree of cumulative permeability was verified through symptoms, physical examination and control vascular ultrasound at each follow-up visit. The data were obtained from the individual medical records of the operated and from a data collection form previously prepared.

They were taken to an Excel database, for further processing in SPSS version 15.0 for Windows. The results were presented in a table and graphs for a better understanding.

## V. RESULTS

Neutrophile-Lymphocyte Index in Patients with Peripheral Arterial Disease Vascular  
Cardiocentral Surgery Service  
2017-2020  
Age and Sex

Table 1

Age and Sex	#	%
Under 40 years old	9	4,4
41 a 50	18	8,9
51 a 60	71	34,8
61 a 70	73	35,7
More than 70 years	33	16,2
Total	204	100.0
Male	129	63,2
Female	75	36,8
Total	204	100,0

Fte. C H

Table # 1 shows us that the highest number of cases was in the 6th and 7th decade of life, with 71 and 73 for 34.8% and 35.7% respectively, with the male sex predominant in 63.2 %, a primary characteristic in

patients with peripheral arteriopathies with a predominance of arteriosclerosis as an etiological factor. The results of the study agree with the majority of the authors reviewed.<sup>1-12</sup>

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Proceed Revascularizing and Predominating Risk Level According to Inl

Table 2

Proceed Revascularizer	Risk Level Pre Surgical			Risk Level Post Surgical			#	%
	<i>L</i>	<i>I</i>	<i>H</i>	<i>L</i>	<i>I</i>	<i>H</i>		
<i>FEMORO-POPLITEAL B/P</i>	28	30	18	55	15	6	76	37,6
<i>CAROTIDA TET</i>	17	15	11	25	11	7	43	21,3
<i>ILIO-FEMORAL B/P</i>	8	5	3	10	4	2	16	7,8
<i>ILIO-ILIAL B/P</i>	4	5	3	6	3	3	12	5,7
<i>SIMPATECTOMY</i>	5	3	3	2	5	4	11	5,3
<i>AXILO-BIFEMORAL B/P</i>	1	3	6	3	4	3	10	4,9
<i>ACUTE THROMBOSIS</i>	5	3	2	1	6	3	10	4,9
<i>CROSS OVER</i>	2	4	3	2	3	4	9	4,3
<i>AORTO-BIFEMORAL B/P</i>	1	2	3	2	3	1	6	2,9
<i>ANEURYSMS</i>	0	5	1	1	4	1	6	2,9
<i>EAGLE SYNDROME</i>	4	1	0	5	0	0	5	2,4
<b><i>TOTAL</i></b>	<b>75</b>	<b>76</b>	<b>53</b>	<b>112</b>	<b>58</b>	<b>34</b>	<b>204</b>	<b>100</b>

Fte.C.H

Table 2 shows the revascularization procedures led by the By Pass techniques and within them the femoro-popliteal with 76 cases for 37.6%, followed by the ilio-femoral, ilio-iliac and axillo-femoral with 16, 12 and 10 cases respectively. Carotid endarterectomy 23 cases with 21.1%. Aortic aneurysms 6 cases for 2.9%.

It should be noted the presence of 5 cases diagnosed as Eagle Syndrome (Compression of the carotid artery by a long and developed styloid process) which underwent resection of the process and repair of vascular damage Regarding the level of risk based on IN / L in the pre-surgical stage, 75 cases were evaluated as low (<2), while the intermediate (2-3) 76 and the high (> 3) with 53, totaled 129 cases for 63.2%, which shows the level of risk of cases with peripheral arteriopathies that require a surgical procedure, revascularization or not.

The analysis of these risk levels in the postoperative period showed the highest number of cases in the low level with 112 for 54.9%, demonstrating the adequate selection of treatment. The intermediate risk level with 58 and the high level with 34 respectively for 92 cases in total allowed us to follow up the cases,

their degree of response and assessment of prediction of complications.

With the analysis of the INL in a serial way, we were able to evaluate the level of risk and the effectiveness of the surgical procedure performed.

Neutrophile-Lymphocyte Index in Patients with Peripheral Arterial Disease  
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2017-2020.

Analysis of the Indices by Date of Carried Out and # Of Cases

Table 3

INL	Pre. Operative	24 Hours	15 days	30 days	60 days	90 days	More 365 days
0-1	24	21	26	38	43	44	55
1-2	51	70	88	115	124	128	130
2-3	76	35	38 sepsis (5)	25	18	18	3 Thrombosis Late 4
3-4	14	31 Thrombosis acute 2	25	15	13	10 2 sepsis Prótesis	7
4-5	16	32	19 Thrombosis (1)	8	4 Thrombosis (1)	0	5
More than 5	23	15 Deceased (2)	8	2 Thrombosis (1early) 3	2	4 Amputated (2)	3 Occlusion C. Mothers Amputated (1)
Total	204	204	204	204	204	204	204

Fte.C.H.

The analysis of the sensitivity and specificity of different levels of the neutrophil / lymphocyte index made it possible to generate 3 risk groups: - low risk with a neutrophil / lymphocyte ratio  $<2$  -Intermediate risk with a neutrophil / lymphocyte ratio between 2 - 3 - high risk with a neutrophil / lymphocyte ratio  $>3$ .

Regarding the N / L index, in the pre-operative low risk 36.7%, intermediate 37.7% and high risk 25.4%, low risk with 54.9%, a decrease in intermediate at 28.4% and high at 16.6% In the first 24 hours after revascularization, a greater number of cases with increased INL was observed, returning to low-risk levels after 15 days, remaining in this range at 30, 60, 90 and more than 360 days after revascularization.

It should be noted that in those cases in which complications occurred, the INL rose above 3, as well as in the two amputees, the INL rose above 5. In general, the longer the surgery time and the low-risk indexes, the cumulative patency was higher in number of cases, as well as when the index showed an increase at high risk, complications became evident

The analysis of the N / L indices in the pre-operative phase, 75 cases for 36.7% was less than 2,

considered as low. The intermediate, that is, between 2-3 was presented in 76 cases for 37.2%, while the high risk level was presented in 53 cases distributed in: level 3-4, 14 cases, between 4-5 16 cases and in more than 5, 23 cases. It should be noted that when the INL level is so high, mortality and morbidity rise regardless of the procedure to be performed. The postoperative period was divided into: at 24 hours, at 15, 30, 60, 90 and 365 days after the operation, highlighting that in general with the therapeutic procedure carried out, the low INL levels were increasing. Complications appeared at the intermediate level (INL 2-3) at 15 days with 5 sepsis and with more than 365 days with 4 late thromboses, which would explain the progressive nature of arteriosclerosis, maximum when the indicated level of prevention is not performed. At high risk levels (INL  $>3$ ) at 24 hours 2 acute thromboses, another at 15 and 60 days, with 2 prosthesis sepsis at 90 days. When the INL level reached 5 or more, at 24 hours there were 2 deaths, at 30 days, 2 thromboses, at 90 days 2 amputees and with more than 365 days, 1 acute occlusion, 1 amputee. As can be seen, the most frequent complication was thrombosis of the revascularization procedure. It should



be noted that in the period studied, mortality was 0.98 with two deaths in the first 24 hours of the procedure performed where the IN / L was always above 5. A cumulative patency of 89.7% was achieved.

## VI. DISCUSSION

Currently all the authors reviewed <sup>(1-12)</sup> coincide in pointing out the participation of neutrophils and lymphocytes in the inflammatory processes that participate in the etiology, presentation and evolution of many diseases, where their inflammatory character determines their levels of lethality and morbidity and mortality <sup>(5-6)</sup>. Based on these concepts, it has been determined that the measurement of the neutrophil-lymphocyte index (IN / L) is a determining factor as a risk marker for these entities and that its knowledge, monitoring and control of existing endothelial dysfunction enables us a higher quality action in the control of these diseases. Authors such as Corriere, Halazun, Aquino Viza and Suilbert Rodríguez <sup>(5-8)</sup> they set the index values to: less than 2 and classify it as low risk; between 2 and 3 as medium or intermediate risk and above 3 as high risk. Rodríguez Blanco <sup>(8)</sup> in his work concludes that the increase in the N / L index greater than 2 is directly related to the presence and severity of coronary artery disease, similar results achieved in this study but related to peripheral artery disease (8). C Chan et al. <sup>(3)</sup> show the prognostic value of the neutrophil / lymphocyte index in patients with critical ischemia in the lower limbs and point out that its increase above 2 is a determining factor in the appearance of complications in these cases with peripheral arterial disease in critical ischemia. Our series shows identical results since complicated cases, which failed and lost their cumulative patency, coincided with the elevation of the index in values above 2 We consider that the continued study of the neutrophil-lymphocyte relationship will allow us to establish indices for our population that requires revascularization for peripheral arterial disease. Its prognostic value is extremely useful in the prevention of morbidity and mortality and amputations, and in turn allows us to predict reaching high levels of cumulative patency. The results obtained, its low cost since it does not require expenses in additional studies, reagents or diagnostic means and the ease in its interpretation, endorse the method and make it extremely useful in the Vascular Surgery services of the Country. All these complications appeared independent of the follow-up of all cases with levels of anti-aggregation and / or anticoagulation, warm-prophylaxis that is part of the care protocol for these patients.

### Conflicts of Interest and Level of Participation

There are no conflicts of interest between the authors of the work.

### Participation Level

Dr. Rubén Tomas Moro Rodríguez.

Main author of the work and promoter of the same

Dr. José Luis Valdés Cantero.

He collaborated in the follow-up of the cases in external consultation and in admitted cases, as well as in the preparation of the work

Dra. Daylin Ricardo Olivera participated in the collection of the data and in the preparation of the work

Dra. Ana María Correa participated in carrying out the laboratory studies, data collection and preparation of the work

Dr. Juan E. Yara Sánchez. He participated as an advisor and consultant of the work

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