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RESEARCH ARTICLE

# Prognostic value of leukocyte-glycemic index in long-term evolution of diabetic patients with peripheral arterial disease following endovascular treatment

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**Objective**: The aim of this article is to determine the predictive value of the leukocyte-glycemic index in the long-term evolution of diabetic patients with peripheral arterial disease following endovascular treatment.
**Methods**: This retrospective observational study enrolled 127 diabetic patients diagnosed with peripheral arterial disease requiring endovascular treatment. Patients were categorized into two groups based on the severity of the infrapopliteal atherosclerotic lesions identified during the pre-operative Computer Tomography Angiography examination. Group 1 includes patients without severe damage to the infrapopliteal artery, while Group 2 includes patients with severe infrapopliteal artery damage, identified by stenosis greater than 70% on all infrapopliteal arteries. The primary outcome was to assess the association between leukocyte-glycemic index value at baseline and the severity of infrapopliteal atherosclerotic lesions and long-term major amputation after percutaneous transluminal angioplasty.
**Results**: Patients in Group 2 had a higher incidence of cardiovascular events (p=0.009), stage IV Leriche-Fontaine (p=0.016), and incidence of major amputation (p<0.001), as well as an increased value of leukocyte-glycemic index (p=0.004). During the follow-up, patients with above-median leukocyte-glycemic index value have a higher risk of major amputation (p=0.034), as seen in the Kaplan-Meier analysis. Moreover, at cox-regression, elevated biomarker values were associated with long-term risk of major amputation, independent of age, sex, cardiovascular risk factors, and below-the-knee arterial occlusion (HR:2.69, p=0.001).
**Conclusions**: Elevated values of leukocyte-glycemic index are associated with the severity of infrapopliteal atherosclerotic lesions and major amputation in the long term.

**Keywords**: leukocyte-glycemic index, vascular surgery, endovascular treatment, peripheral arterial disease

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## Introduction

Peripheral arterial disease (PAD) is a condition in which the arteries that supply blood to the lower limb become narrowed, caused by the presence of atherosclerotic plaques, leading to a decrease in blood flow [1]. Depending on the severity of the disease and the Leriche-Fontaine classification [2], patients may experience claudication pain during physical activity (Stages I-II), which can worsen to pain at rest (Stage III) and trophic lesions in advanced stages (Stage IV). Patients in stages III and IV Leriche Fontaine are at a high risk of major amputation due to severe atherosclerotic lesions and limited options for surgical or endovascular revascularization [1–4].

Among the main risk factors that predispose and aggravate atherosclerotic lesions are cardiovascular comorbidities [5], diabetes mellitus (DM) [6], and active smoking [7]. In addition, patients who have PAD and DM are at a higher risk of major amputation and mortality compared to those without DM [8, 9]. According to a study by Danielsson et al. [10]recognized as an inflammatory disease of the vessel wall, probably accelerated by DM patients with critical limb ischemia (CLI) and DM have higher levels of interleukin-6 and white blood cells (WBC) compared to those without DM. Moreover, a recent study by Mureșan et al. [11] found that high levels of systemic inflammatory markers are linked to the presence of subclinical atherosclerosis in patients with diabetic polyneuropathy. Due to the high risk of unfavorable progression in patients with PAD, several inflammatory biomarkers with prognostic value have been proposed and analyzed [3, 5, 10–12]and is the most common manifestation of the atherosclerotic process, except for the coronary and cerebral arterial systems. Inflammation is well known to have a role in the progression of atherosclerosis and, by extension, in PAD. Among the recently studied markers in the literature, we

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list the neutrophil–lymphocyte ratio (NLR, but none have been implemented in medical practice yet.

In 2010, Quiroga Castro et al. [13] proposed a new inflammatory biomarker called leuko-glycemic index (LGI) to understand better the accuracy of the atherosclerotic process and the presence of DM. LGI is based on the count of leukocytes and glycemic value [13–17]. Several articles have demonstrated the prognostic role of LGI in assessing the severity of coronary atherosclerotic lesions and the evolution of patients with ST-elevation myocardial infarction (STEMI) [14–17]. More Recently, Mureșan et al. [17] found that high baseline LGI values are linked to arteriovenous fistula dysfunction in the long term.

The aim of this article is to determine the predictive value of LGI in evaluating the extent of atherosclerotic lesions in the infrapopliteal arteries and the long-term risk of major amputation in diabetic patients with PAD who undergo percutaneous transluminal angioplasty.

## Methods

### Study Design

This is a retrospective observational study that enrolled all diabetic patients diagnosed with peripheral arterial disease requiring endovascular treatment and admitted to the Vascular Surgery Clinic of Targu Mures County Emergency Clinic Hospital between January 2019 and June 2023. Patients with autoimmune or hematological diseases, patients requiring additional revascularization surgery during hospitalization, and patients lost during the follow-up call were excluded from the study. Patients were categorized into two groups based on the severity of the infrapopliteal atherosclerotic lesions identified during the pre-operative Computer Tomography Angiography (CTA) examination. Group 1 includes patients without severe damage to the infrapopliteal artery, while Group 2 includes patients with severe infrapopliteal artery damage, identified by stenosis greater than 70% on all three infrapopliteal arteries.

This study was approved by the Medical Ethics Committee for the Clinical Study of Medicines of the County Emergency Clinical Hospital Târgu Mureș, decision number no. 31326/27.11.2023.

### Data Collection

Demographic data, routine laboratory analyses, patient comorbidities (hypertension, ischemic heart disease, chronic heart failure, cardiovascular events, cerebrovascular events, and varicose veins), and risk factors (obesity, active smoking, and dyslipidemia) were retrieved from the hospital's electronic database. Cardiovascular events were defined as a history of myocardial infarction or angina pectoris, and cerebrovascular events were defined as a history of stroke or transient ischemic attack. In addition, the pre-operative CTA examination quantified infrainguinal atherosclerotic lesions in the common femoral artery (CFA), superficial femoral artery, popliteal artery (PA), anterior tibial artery, posterior tibial artery, and peroneal artery. The lesions were classified as hemodynamically significant stenoses (70%-90%), sub-occlusive stenoses (90%-99%), and occlusions. LGI was calculated using the formula from the literature [17]: (Leukocyte count x$10^3$/uL) multiplied by (glucose level in mg/dL) divided by 1000.

### Study Outcome

The primary outcome was to assess the association between LGI value at baseline and risk of major amputation in the long term after endovascular revascularization. Patients were contacted by phone between January 2024 and February 2024 to determine the risk of amputation in the long term after the surgery. On average, patients were followed up for a period of 1.41±0.93 years after being discharged from the hospital. As a secondary outcome, we investigated the association between LGI values and the severity of infrainguinal atherosclerotic lesions.

### Statistical analysis

The statistical analysis for this study was conducted using SPSS for Mac OS version 28.0.1.0 developed by SPSS, Inc. in Chicago, IL, USA. The average age, laboratory data, follow-up period, and length of stay (LOS) were presented as mean values with standard deviation (SD). For dichotomous variables, we used chi-square tests to compare characteristics between groups, while for continuous variables, we used Mann-Whitney and Student's t-tests to assess differences. We used ROC curve analysis to determine appropriate cut-off values for leukocytes, admission glucose level, neutrophils, and LGI based on the Youden index, which ranges from 0 to 1 and is calculated as Youden Index = Sensitivity + Specificity – 1. We used multivariate Cox proportional hazard analyses to identify independent predictors of major amputation risk in diabetic patients. Moreover, HR was expressed per 1 SD increase in the baseline for all laboratory data analyzed. Furthermore, we used 3 different adjustment models to assess the associations between neutrophil and LGI and major amputation. Thus, Model 1 includes age and sex; Model 2 includes age, sex, and cardiovascular risk factors (hypertension, smoking, obesity, dyslipidemia, Stage IV Leriche-Fontaine), and Model 3 which additionally includes below-the-knee arterial occlusion. Kaplan-Meier curves were used to model the crude association between LGI and major amputation risk. The Log Rank test was used to compare the curves. All tests were two-tailed, and a p-value less than 0.05 was considered statistically significant.

## Results

We conducted a study that involved 127 diabetic patients with PAD, whose average age was 67.82±8.39. Among these patients, 81.10% were men. After analyzing comorbidities and risk factors, we found that patients in Group 2 had a higher incidence of cardiovascular events (p=0.009), a higher incidence of stage IV Leriche-Fontaine (p=0.016), and a lower incidence of stage II Leriche-Fontaine (p=0.004) (Ta-

ble I). We also observed a higher rate of major amputation in the same group of patients (p<0.001) (Table I).

At laboratory analysis, Group 2 patients had an increased number of WBC (p=0.029), glucose (p=0.016), neutrophils (p=0.017), and LGI (p=0.004). They also had a lower number of lymphocytes (p<0.001) (Table I).

Furthermore, at the pre-operative CTA analysis, in the group of patients with severe atherosclerotic damage of the infrapopliteal arteries, we observed a higher incidence of CFA occlusion (p=0.008) and PA occlusion (p=0.023), as well as sub-occlusions and occlusions of the infrapopliteal arteries (for all p<0.001) (Table II). Additionally, we did not observe a statistically significant difference for a single artery (p=0.914) but found a higher incidence for two (p=0.006) and three arteries (p<0.001) regarding the number of occluded arteries below the knee (Table II).

Additionally, Table III shows that neutrophils (AUC: 0.682, p=0.005), glucose (AUC: 0.629, p=0.035), and LGI (AUC: 0.729, p<0.001) are associated with the long-term risk of major amputation according to the ROC analysis.

During the follow-up, patients with above-median LGI value at baseline have a higher risk of major amputation (p=0.034), as seen in Figure 1 using Kaplan-Meier analysis.

To identify the prognostic factors of major amputation, we conducted cox-regression analysis. As presented in Table IV, the number of neutrophils (HR: 1.71, p=0.046) and LGI (HR: 2.55, p<0.001) were only associated with the analyzed outcome.

We subjected the two variables mentioned earlier to three adjustment models, as shown in Table 5. After adjusting for models 2 and 3, the number of neutrophils no longer showed a statistically significant association with the risk of major amputation. However, high baseline values for LGI were associated with long-term risk of major amputation, independent of age, sex, cardiovascular risk factors, and below-the-knee arterial occlusion (Model 3: HR: 2.69, p=0.001) (Table V).

## Discussions

This study's main finding is that elevated basal values of LGI are associated with the severity of infrapopliteal atherosclerotic lesions and with the risk of major amputation in the long term, independently of age, sex, cardiovascular risk factors, and below-the-knee arterial occlusion.

**Table I. All characteristics of patients enrolled in this study presented for the entire cohort and according to the presence of severe atherosclerotic lesions for the infrapopliteal arteries.**

| Variables | All Patients n=127 | Group 1 n=109 | Group 2 n=18 | p value |
|---|---|---|---|---|
| Age mean ± SD | 67.82±8.39 | 67.33±8.15 | 70.77±9.41 | 0.158 |
| Male no. (%) | 103 (81.10%) | 88 (80.73%) | 15 (83.33%) | 0.794 |
| **Comorbidities and Risk factors, no. (%)** | | | | |
| Hypertension | 106 (83.46%) | 90 (82.57%) | 16 (88.89%) | 0.504 |
| Ischemic Heart Disease | 70 (55.12%) | 59 (54.13%) | 11 (61.11%) | 0.581 |
| Chronic Heart Failure | 40 (31.50%) | 34 (31.19%) | 6 (33.33%) | 0.856 |
| Atrial Fibrillation | 15 (11.81%) | 12 (11.01%) | 3 (16.67%) | 0.732 |
| Cardiovascular events | 19 (14.96%) | 12 (11.01%) | 7 (38.89%) | **0.009** |
| Cerebrovascular events | 14 11.02%) | 10 (9.17%) | 4 (22.22%) | 0.102 |
| Varicose Veins | 10 (7.87%) | 8 (7.34%) | 2 (11.11%) | 0.582 |
| Obesity | 42 (33.07%) | 33 (30.28%) | 9 (50.0%) | 0.099 |
| Active Smoking | 65 (51.18%) | 53 (48.62%) | 12 (66.67%) | 0.063 |
| Dyslipidemia | 69 (54.33%) | 59 (54.13%) | 10 (55.56%) | 0.581 |
| **Laboratory data, mean ± SD** | | | | |
| WBC | 9.13±2.44 | 8.83±2.09 | 10.81±3.49 | **0.029** |
| BUN (mg/dL) | 45.92±21.95 | 45.20±22.22 | 50.42±20.25 | 0.193 |
| Creatinine (mg/dL) | 1.19±1.11 | 1.21±1.18 | 1.05±0.36 | 0.926 |
| eGFR ml/min/1,73 $m^2$ | 80.72±29.58 | 80.34±29.23 | 83.16±32.60 | 0.815 |
| Glucose (mg/dL) | 145.35±61.36 | 142.94±65.15 | 159.13±29.57 | **0.016** |
| Hemoglobin g/dL | 12.82±1.87 | 12.91±1.91 | 12.35±1.64 | 0.159 |
| Hematocrit % | 38.37±5.19 | 38.76±5.27 | 36.19±4.22 | 0.071 |
| Neutrophils x$10^3$/uL | 6.00±1.56 | 5.84±1.50 | 6.90±1.62 | **0.017** |
| Lymphocytes x$10^3$/uL | 2.01±0.81 | 2.10±0.81 | 1.42±0.55 | **<0.001** |
| Monocyte x$10^3$/uL | 0.70±0.25 | 0.71±0.25 | 0.65±0.24 | 0.153 |
| PLT x$10^3$/uL | 264.05±94.51 | 270.48±93.02 | 227.24±97.24 | 0.060 |
| LGI | 1.35±0.59 | 1.29±0.58 | 1.71±0.53 | **0.004** |
| **Leriche-Fontaine Classification, no. (%)** | | | | |
| IIB | 61 (48.03%) | 58 (53.21%) | 3 (16.67%) | **0.004** |
| III | 32 (25.20%) | 26 (23.85%) | 6 (33.33%) | 0.391 |
| IV | 34 (26.77%) | 25 (22.94%) | 9 (50.0%) | **0.016** |
| PTA Stent, no. (%) | 43 (33.86%) | 40 (36.70%) | 3 (16.67%) | 0.108 |
| PTA Balloon, no. (%) | 84 (66.14%) | 69 (63.30%) | 15 (83.33%) | |
| Major Amputation, no. (%) | 14 (11.02%) | 5 (4.59%) | 9 (50.0%) | **<0.001** |
| Follow-up period (years) mean ± SD | 1.41±0.93 | 1.46±0.98 | 1.11±0.44 | 0.059 |
| Length of Stay (days) mean ± SD | 5.62±4.06 | 5.89±4.24 | 4.00±2.11 | 0.338 |

SD = standard deviation; WBC = white blood cells; BUN = blood urea nitrogen; PLT = platelet count; LGI = leuko-glycemic index; PTA = percutaneous transluminal angioplasty.

Table II. The severity of atherosclerotic lesions at the level of the infrainguinal arteries presented for the entire cohort and according to the presence of severe atherosclerotic lesions for the infrapopliteal arteries.

| Variables | | All Patients n=127 | Group 1 n=109 | Group 2 n=18 | p value |
|---|---|---|---|---|---|
| Common Femoral Artery | 70-90% | 9 (7.09%) | 8 (7.34%) | 1 (5.55%) | 0.785 |
| | 90-99% | 6 (4.72%) | 4 (3.67%) | 2 (11.11%) | 0.168 |
| | Occlusion | 3 (2.36%) | 1 (0.92%) | 2 (11.11%) | **0.008** |
| Superficial Femoral Artery | 70-90% | 13 (10.24%) | 11 (10.09%) | 2 (11.11%) | 0.895 |
| | 90-99% | 20 (15.57%) | 16 (14.68%) | 4 (22.22%) | 0.416 |
| | Occlusion | 22 (17.32%) | 19 (17.43%) | 3 (16.67%) | 0.937 |
| Popliteal Artery | 70-90% | 3 (2.36%) | 2 (1.83%) | 1 (5.55%) | 0.336 |
| | 90-99% | 12 (9.45%) | 11 (10.09%) | 1 (5.55%) | 0.542 |
| | Occlusion | 15 (11.81%) | 10 (9.17%) | 5 (27.78%) | **0.023** |
| Anterior Tibial Artery | 70-90% | 5 (3.94%) | 4 (3.67%) | 1 (5.56%) | 0.703 |
| | 90-99% | 12 (9.45%) | 5 (4.59%) | 7 (38.89%) | **<0.001** |
| | Occlusion | 28 (22.05%) | 18 (16.05%) | 10 (55.55%) | **<0.001** |
| Posterior Tibial Artery | 70-90% | 3 (2.36%) | 2 (1.83%) | 1 (5.55%) | 0.336 |
| | 90-99% | 4 (3.15%) | 3 (2.75%) | 1 (5.55%) | 0.528 |
| | Occlusion | 41 (32.28%) | 25 (22.94%) | 16 (88.89%) | **<0.001** |
| Peroneal Artery | 70-90% | 3 (2.36%) | 3 (2.75%) | - | 0.143 |
| | 90-99% | 7 (5.51%) | 3 (2.75%) | 4 (22.22%) | **<0.001** |
| | Occlusion | 19 (14.96%) | 6 (5.50%) | 13 (72.22%) | **<0.001** |
| Below-the-Knee Arterial Occlusion | 1 | 27 (21.26%) | 23 (21.10%) | 4 (22.22%) | 0.914 |
| | 2 | 20 (15.75%) | 13 (11.93%) | 7 (38.89%) | **0.006** |
| | 3 | 7 (5.51%) | - | 7 (38.89%) | **<0.001** |

Table III. ROC analysis characteristics for WBC count, glucose levels, neutrophils, and LGI regarding Major Amputation.

| Variables | Cut-Off | AUC | Std. Error | 95% CI | Sensitivity | Specificity | p value |
|---|---|---|---|---|---|---|---|
| WBC | - | 0.651 | 0.077 | 0.500-0.802 | - | - | 0.051 |
| Neutrophil | 6.13 | 0.682 | 0.065 | 0.555-0.809 | 84.6% | 59.8% | **0.005** |
| Glucose | 124.5 | 0.629 | 0.061 | 0.509-0.749 | 92.3% | 45.8% | **0.035** |
| LGI | 1.28 | 0.729 | 0.063 | 0.606-0.853 | 76.9% | 58.9% | <0.001 |

AUC =area under curve; CI = confidence interval; WBC = white blood cells; LGI = leuko-glycemic index

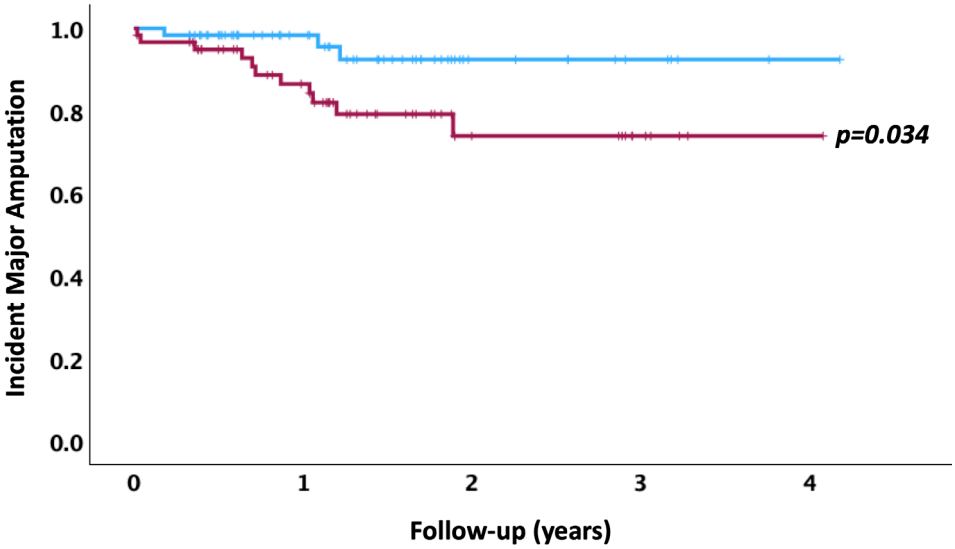


Fig. 1. Kaplan-Meier curves for incident amputation in the entire cohort by the median value of LGI at baseline. The p-value was calculated using an unadjusted log-rank test.

The relationship between the atherosclerotic process and systemic inflammation is well known, and the role of inflammatory biomarkers in the unfavorable evolution of PAD and carotid disease has been demonstrated in numerous articles published in the literature[3, 5, 10–12, 18]and is the most common manifestation of the atherosclerotic process, except for the coronary and cerebral arterial systems. Inflammation is well known to have a role in the progression of atherosclerosis and, by extension, in PAD. Among the recently studied markers in the literature, we list the neutrophil–lymphocyte ratio (NLR. However, depending on the patient cohort enrolled, the authors proposed different threshold values with a significant dispersion, which is why they are not currently used in medical practice [19].

Quiroga Castro et al. [13] were the first to demonstrate that high LGI values are linked to the risk of mortality and heart failure within 30 days among STEMI patients.

Table IV. Correlations between comorbidities, baseline laboratory data, and follow-up major amputation risk.

| Variables | | Major Amputation | | |
|---|---|---|---|---|
| | | HR | 95%CI | p value |
| Male | | 3.25 | 0.42-24.58 | 0.260 |
| Age | | 1.51 | 0.84-2.65 | 0.165 |
| Cardiovascular Events | | 1.31 | 0.89-1.93 | 0.159 |
| Cerebrovascular Events | | 2.03 | 0.56-7.28 | 0.279 |
| Obesity | | 1.14 | 0.61-2.14 | 0.677 |
| Active Smoking | | 2.75 | 0.95-7.96 | 0.062 |
| Dyslipidemia | | 1.50 | 0.50-4.48 | 0.467 |
| Leriche-Fontaine Classification | IIB | 0.62 | 0.21-1.85 | 0.391 |
| | III | 1.16 | 0.36-3.71 | 0.799 |
| | IV | 1.49 | 0.50-4.45 | 0.474 |
| PTA Stent | | 0.29 | 0.06-1.32 | 0.109 |
| WBC | | 1.28* | 0.85-2.88 | 0.179 |
| Neutrophil | | 1.71* | 1.01-2.89 | **0.046** |
| Glucose | | 1.48* | 0.95-2.28 | 0.079 |
| LGI | | 2.55* | 1.51-4.30 | **<0.001** |

HR = hazard ratio; CI = confidence interval; PTA = percutaneous transluminal angioplasty; WBC = white blood cells; PLT = platelet count; LGI = leuko-glycemic index. *HR expressed per 1 SD increase in baseline.

Table V. Cox-regression analysis: the association of Neutrophil count and LGI at baseline and Major Amputation.

| Biomarker | Model | Major Amputation | | |
|---|---|---|---|---|
| | | HR* | 95%CI | p value |
| Neutrophil | Model 1 | 1.84 | 1.01-3.40 | **0.048** |
| | Model 2 | 1.64 | 0.97-2.76 | 0.064 |
| | Model 3 | 1.51 | 0.76-2.98 | 0.241 |
| LGI | Model 1 | 2.61 | 1.59-4.28 | **<0.001** |
| | Model 2 | 2.71 | 1.56-4.73 | **<0.001** |
| | Model 3 | 2.69 | 1.49-4.86 | **0.001** |

HR = hazard ratio; CI = confidence interval; LGI = leuko-glycemic index. *HR expressed per 1 SD increase in baseline. Model 1: age and sex; Model 2: age, sex, cardiovascular risk factors (hypertension, smoking, obesity, dyslipidemia, Stage IV Leriche-Fontaine); Model 3: age, sex, cardiovascular risk factors (hypertension, smoking, obesity, dyslipidemia, Stage IV Leriche-Fontaine), and below-the-knee arterial occlusion.

Similarly, Hirschson Prado et al. [14] showed that LGI is a predictive factor of in-hospital mortality based on a study of 405 patients with STEMI. Later, León-Aliz et al. [15] identified a threshold value of 1.158 for LGI and a 3 times higher mortality risk among STEMI patients with a biomarker value exceeding this threshold. More recently, Peker et al. [20], in an observational, retrospective study that enrolled 546 patients with coronary total occlusion, found that LGI is a predictive factor of all-cause mortality (OR: 1.05, p=0.02).

Furthermore, Seoane et al. [21] validated previous results on a cohort of 3813 patients who underwent coronary artery bypass surgery. The study analyzed the risk of in-hospital mortality, acute kidney injury, or low cardiac output. Using multivariate logistic regression analysis, the authors found that LGI is a predictive factor of the above-mentioned endpoint (OR: 1.508, p<0.001) [21]. Our team has recently published a research paper that analyzes the impact of LGI on long-term arteriovenous fistula failure. The study conducted by Mureșan et al. [17] discovered that an increased baseline value of LGI can predict vascular access dysfunction independent of demographic data, pre-operative mapping, or cardiovascular risk factors (HR: 3.49, p=0.037).

The current study has some limitations that must be mentioned. Firstly, it is a retrospective study on patients enrolled from a single center. Secondly, we only included patients who underwent endovascular treatment, so our findings cannot be generalized to patients who underwent surgical revascularization. Finally, patients were only examined pre-operatively by CTA, and follow-up investigations were not performed.

## Conclusion

In conclusion, elevated baseline values of LGI are associated with the severity of infrapopliteal atherosclerotic lesions and with the risk of major amputation in the long term. The predictive role of LGI is independent of age, sex, cardiovascular risk factors, and below-the-knee arterial occlusion.

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## Authors' contribution

AVM (Conceptualization; Methodology; Project administration; Validation; Visualization; Writing – original draft; Supervision)
EMA (Conceptualization; Data curation; Formal analysis; Investigation; Software; Validation; Writing – original draft)
RK (Formal analysis; Investigation; Resources)
LM (Data curation; Investigation; Resources)
BAC (Data curation; Formal analysis; Investigation; Resources)
CCC (Formal analysis; Methodology; Writing – review & editing)
ER (Project administration; Resources; Validation; Visualization; Supervision; Writing – review & editing)

## Conflict of interest

None to declare.

## References

1. Nordanstig J, Behrendt C-A, Baumgartner I, et al. Editor's Choice -- European Society for Vascular Surgery (ESVS) 2024 Clinical Practice Guidelines on the Management of Asymptomatic Lower Limb Peripheral Arterial Disease and Intermittent Claudication . Eur J Vasc Endovasc Surg. 2024;67(1):9–96.
2. Fontaine R, Kim M, Kieny R. [Surgical treatment of peripheral circulation disorders]. Helv Chir Acta. 1954;21(5–6):499–533.
3. Russu E, Mureșan AV, Arbănași EM, et al. The Predictive Role of NLR and PLR in Outcome and Patency of Lower Limb Revascularization in Patients with Femoropopliteal Disease. J Clin Med. 2022;11(9):2620.
4. Russu E, Mureșan AV, Ivănescu AD, et al. Polytetrafluorethylene (PTFE) vs. Polyester (Dacron®) Grafts in Critical Limb Ischemia Salvage. Int J Environ Res Public Health. 2023;20(2):1235.
5. Derșidan AA, Ciucanu CC, Ilioniu AM, et al. Neutrophil-to-Lymphocyte Ratio and Systemic Inflammation Index as Predictors of Poor Outcome in Patients with Critical Limb Ischemia Treated with Remote Endarterectomy. J Cardiovasc Emergencies. 2022;8(4):67–74.

6. Giannopoulos S, Armstrong EJ. Diabetes mellitus: an important risk factor for peripheral vascular disease. Expert Rev Cardiovasc Ther. 2020;18(3):131–7.
7. Lu Q, Wang J, Wei X, Wang G, Xu Y. Risk Factors for Major Amputation in Diabetic Foot Ulcer Patients. Diabetes Metab Syndr Obes Targets Ther. 2021;14:2019–27.
8. Keller K, Schmitt VH, Vosseler M, et al. Diabetes Mellitus and Its Impact on Patient-Profile and In-Hospital Outcomes in Peripheral Artery Disease. J Clin Med. 2021;10(21):5033.
9. Pourghaderi P, Yuquimpo KM, Roginski Guetter C, Mansfield L, Park HS-M. Outcomes following Lower Extremity Amputation in Patients with Diabetes Mellitus and Peripheral Arterial Disease. Ann Vasc Surg. 2020;63:259–68.
10. Danielsson P, Truedsson L, Eriksson KF, Norgren L. Inflammatory markers and IL-6 polymorphism in peripheral arterial disease with and without diabetes mellitus. Vasc Med Lond Engl. 2005;10(3):191–8.
11. Mureşan AV, Tomac A, Opriş DR, et al. Inflammatory Markers Used as Predictors of Subclinical Atherosclerosis in Patients with Diabetic Polyneuropathy. Life. 2023;13(9):1861.
12. Demirdal T, Sen P. The significance of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and lymphocyte-monocyte ratio in predicting peripheral arterial disease, peripheral neuropathy, osteomyelitis and amputation in diabetic foot infection. Diabetes Res Clin Pract. 2018;144:118–25.
13. Castro WA, Conci E, Zelaya F, Isa M, Pacheco G, Sala J. Estratificación del riesgo en el infarto agudo de miocardio según el índice leucoglucémico ¿El «Killip-Kimball» de laboratorio? Rev Fed Arg Cardiol. 2010;39:29–34.
14. Hirschson Prado A, Higa C, Merlo P, 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.
15. León-Aliz E, Moreno-Martínez FL, Pérez-Fernández GA, Vega-Fleites LF, Rabassa-López-Calleja MA. [Leuko-glycemic index as an in-hospital prognostic marker in patients with ST-segment elevation myocardial infarction]. Clin E Investig En Arterioscler Publicacion Of Soc Espanola Arterioscler. 2014;26(4):168–75.
16. Rodríguez Jiménez A, Fardales Rodríguez R, Toledo Rodríguez E, Quintana Cañizarez G. Índice leuco-glucémico como factor pronóstico tras un infarto agudo del miocardio con elevación del segmento ST. Rev Finlay. 2019;97–107.
17. Mureşan AV, Florea E, Arbănaşi E-M, et al. Elevated Leukocyte Glucose Index Is Associated with Long-Term Arteriovenous Fistula Failure in Dialysis Patients. J Clin Med. 2024;13(7):2037.
18. Niculescu R, Russu E, Arbănaşi EM, et al. Carotid Plaque Features and Inflammatory Biomarkers as Predictors of Restenosis and Mortality Following Carotid Endarterectomy. Int J Environ Res Public Health. 2022;19(21):13934.
19. Lăpădatu BI, Russu E. Neutrophil-to-Lymphocyte Ratio – Risk of Amputation and Mortality in Patients with Limb-Threatening Ischemia – a Systematic Review. J Cardiovasc Emergencies. 2024;10(1):7–12.
20. Peker T, Özbek M, Boyraz B, Aslan SF, Demir M, Aslan B. Prognostic value of the leuko-glycemic index in coronary chronic total occlusion patients. Eur Res J. 2023;9(5):1099–104.
21. Seoane LA, Burgos L, Espinoza JC, et al. Prognostic Value of the Leuko-Glycaemic Index in the Postoperative Period of Coronary Artery Bypass Grafting. Braz J Cardiovasc Surg. 2021;36:484–91.