NEU PRESS

SELCUK MEDICAL JOURNAL
SELÇUK TIP DERGİSİ

DOI:http:/dx.doi.org/10.30733/std.2026.02011
Selcuk Med J 2026;42(3): 308- 315

OPEN

RESEARCH ARTICLE

Pan-Immune-Inflammation Value Is Independently Associated With Vascular Burden in Patients Undergoing Carotid Artery Stenting

Karotis Arter Stentleme Uygulanan Hastalarda Pan-İmmün-İnflamasyon Değerinin Vasküler Yük ile Bağımsız İlişkisi

Tolga Kunak[1], Aysegul Ulgen Kunak[2], Ozkan Kayhan[3]

[1]Akdeniz University, Faculty of Medicine, Department of Cardiology, Antalya, Türkiye
[2]University of Health Sciences, Antalya Training and Research Hospital, Department of Cardiology, Antalya, Türkiye
[3]Kepez State Hospital, Department of Cardiology, Antalya, Türkiye

ABSTRACT

Objective: The pan-immune-inflammation value (PIV) is a composite inflammatory biomarker investigated in cardiovascular diseases. This study evaluated the association between PIV and vascular comorbidity burden in patients undergoing carotid artery stenting (CAS).

Materials and Methods: This retrospective study included 221 patients who underwent CAS between 2010 and 2025. PIV was calculated from peripheral blood cells. Vascular burden comprised hypertension, diabetes mellitus, hyperlipidemia, smoking, coronary artery disease, and previous cerebrovascular events. Patients were categorized into low (0–2) and high (3–5) burden groups. Associations were assessed using correlation and regression analyses, and discrimination by ROC analysis.

Results: PIV was higher in patients with high vascular burden (428.9 [287.1–701.9] vs. 287.1 [202.1–452.5], p=0.001) and correlated positively with vascular burden (rho=0.317, p<0.001). Each 100-unit increase in PIV was independently associated with high vascular burden (OR=1.152; 95% CI: 1.058–1.255; p=0.001). In adjusted ordinal regression, PIV was associated with higher vascular burden (OR=1.116; 95% CI: 1.062–1.174; p<0.001). ROC analysis yielded an AUC of 0.651 (95% CI: 0.577–0.725).

Conclusion: Higher PIV was independently associated with greater vascular comorbidity burden in patients undergoing CAS. However, its modest discriminatory performance limits its use as a standalone risk-stratification tool.

Keywords: Pan-immune-inflammation value, carotid artery stenting, vascular burden, inflammation, atherosclerosis

ÖZET

Amaç: Pan-immün-inflamasyon değeri (PIV), kardiyovasküler hastalıklarda araştırılan bileşik bir inflamatuvar biyobelirteçtir. Bu çalışmada, karotis arter stentleme (KAS) uygulanan hastalarda PIV ile vasküler komorbidite yükü arasındaki ilişkinin araştırılması amaçlandı.

Gereç ve Yöntemler: Retrospektif çalışmaya 2010–2025 yılları arasında KAS uygulanan 221 hasta dahil edildi. PIV periferik kan hücrelerinden hesaplandı. Vasküler yük skoru; hipertansiyon, diabetes mellitus, hiperlipidemi, sigara, koroner arter hastalığı ve geçirilmiş serebrovasküler olaydan oluşan altı bileşenle belirlendi. Hastalar düşük (0–2) ve yüksek (3–5) yük gruplarına ayrıldı. İlişkiler korelasyon ve regresyon analizleriyle, ayırt edici performans ROC analiziyle değerlendirildi.

Bulgular: PIV, yüksek vasküler yük grubunda daha yüksekti (428,9 [287,1–701,9] vs. 287,1 [202,1–452,5], p=0,001). PIV ile vasküler yük arasında pozitif korelasyon vardı (rho=0,317, p<0,001). Her 100 birimlik PIV artışı, yüksek vasküler yük ile bağımsız ilişkiliydi (OR=1,152; %95 GA: 1,058–1,255; p=0,001). Düzeltilmiş ordinal regresyonda PIV, daha yüksek vasküler yük ile ilişkiliydi (OR=1,116; %95 GA: 1,062–1,174; p<0,001). ROC analizinde AUC 0,651 (%95 GA: 0,577–0,725) bulundu.

Sonuç: Yüksek PIV, KAS hastalarında daha yüksek vasküler komorbidite yükü ile bağımsız ilişkilidir. Ancak sınırlı ayırt edici performansı nedeniyle PIV tek başına risk sınıflandırma aracı olarak kullanılmamalıdır.

Anahtar Kelimeler: Pan-immün-inflamasyon değeri, karotis arter stentleme, vasküler yük, inflamasyon, ateroskleroz

Received: 28 June 2026 **Accepted:** 5 September 2026 **Published Online:** 14 September 2026

Corresponding Author: Aysegul Ulgen Kunak, University of Health Sciences, Antalya Training and Research Hospital, Department of Cardiology, Antalya, Türkiye
e-mail: aysegululgen@yahoo.com

Cite this article as: Kunak T, Ulgen Kunak A, Kayhan O. Pan-Immune-Inflammation Value Is Independently Associated With Vascular Burden in Patients Undergoing Carotid Artery Stenting. Selcuk Med J 2026;42(3): 308-315

Disclosure: *Author has not a financial interest in any of the products, devices, or drugs mentioned in this article. The research was not sponsored by an outside organization. Author has agreed to allow full access to the primary data and to allow the journal to review the data if requested.*

INTRODUCTION

Carotid artery stenosis remains an important cause of ischemic stroke and contributes substantially to global cerebrovascular morbidity and mortality despite advances in preventive strategies and revascularization techniques (1,2). Carotid artery stenting (CAS) has emerged as an effective alternative to carotid endarterectomy in selected patients; however, residual vascular risk and recurrent ischemic events continue to represent important clinical challenges, particularly among patients with multiple cardiovascular comorbidities (3–5). Patients undergoing CAS frequently have multiple cardiovascular risk factors and established atherosclerotic comorbidities, reflecting a broader burden of systemic vascular disease that may not be fully captured by the severity of the carotid lesion alone (4–6). Atherosclerosis is increasingly recognized as a chronic inflammatory and immune-mediated vascular disease characterized by endothelial dysfunction, lipid accumulation, oxidative stress, leukocyte recruitment, and platelet activation (7–10). Persistent vascular inflammation contributes to plaque progression, destabilization, and thromboembolic complications through complex interactions involving endothelial cells, monocytes, neutrophils, inflammatory cytokines, and activated platelets (8–11). In addition, residual inflammatory risk has emerged as a major determinant of recurrent cardiovascular and cerebrovascular events despite optimal lipid-lowering therapy (9,12). Recent evidence suggests that persistent inflammation within the vascular microenvironment plays an important role in carotid plaque vulnerability and the pathogenesis of ischemic stroke (10,13).

Platelets are central mediators of thromboinflammation and actively contribute to vascular inflammation, endothelial dysfunction, and atherosclerotic plaque progression (14,15). Beyond their traditional role in thrombosis and hemostasis, activated platelets modulate leukocyte recruitment, cytokine signaling, and immune activation within the vascular microenvironment (11,15). Experimental and translational studies have demonstrated that platelet-mediated inflammatory pathways contribute to atherosclerotic progression and vascular injury (15,16). In recent years, inflammation-based hematologic biomarkers derived from routinely measured blood parameters have attracted increasing interest as practical tools for cardiovascular and cerebrovascular risk assessment (17–19). These include the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), the systemic immune-inflammation index (SII), and the pan-immune-inflammation value (PIV), all of which integrate different circulating immune and hematologic cell populations. Compared with conventional single-parameter inflammatory markers, these composite indices may provide a broader representation of systemic inflammatory and thromboinflammatory activity.

Recent evidence suggests that inflammatory and platelet-related biomarkers are associated with carotid plaque vulnerability and clinical outcomes in patients with carotid artery disease (10,13). In patients undergoing CAS, Keskin et al. demonstrated that SII was independently associated with adverse outcomes (20). Similarly, imaging studies have highlighted the close relationship between inflammatory activity and imaging features of carotid plaque vulnerability (13). Platelet-related biomarkers have also been associated with clinical characteristics and vascular events in patients with atherosclerotic carotid artery stenosis (10,16). More recently, composite nutritional and immune-inflammatory indices have also been investigated as readily available markers of cardiovascular disease burden and risk in other clinical populations, including patients with heart failure with preserved ejection fraction and those undergoing mitral balloon valvuloplasty (21,22). These findings suggest that systemic inflammatory indices may reflect broader cardiovascular disease burden. Most previous studies of patients undergoing CAS have primarily focused on procedural outcomes, cardiovascular or cerebrovascular events, or disease-specific prognostic endpoints, whereas the association between PIV and cumulative vascular comorbidity burden has not been sufficiently characterized. Importantly, the vascular burden score used in the present study reflects the accumulation of major cardiovascular risk factors and established vascular comorbidities rather than anatomical carotid disease burden or stenosis severity. Therefore, the present study aimed to investigate the association between PIV and cumulative vascular comorbidity burden in patients undergoing CAS. We hypothesized that higher PIV levels would be associated with greater cumulative vascular comorbidity burden.

MATERIALS AND METHODS

Design and Participants

This retrospective observational study included 221 consecutive patients who underwent CAS at a tertiary cardiovascular center from 2010 to 2025. The aim of this study was to evaluate the association between systemic inflammatory burden and cumulative vascular comorbidity burden in patients with carotid artery stenosis who underwent CAS. Because follow-up data were not consistently available, the analysis was restricted to baseline demographic, clinical, and laboratory parameters. Patients were eligible if they had undergone CAS for carotid artery stenosis and had the baseline demographic, clinical, and laboratory data required for the present analysis. Patients lacking sufficient baseline data to calculate either PIV or the vascular burden score were excluded. To assess cumulative vascular comorbidity burden, a vascular burden score was constructed based on the presence of major atherosclerotic risk factors and vascular comorbidities, including hypertension, diabetes mellitus, hyperlipidemia, smoking, a history of coronary artery disease, and prior cerebrovascular events. Each variable was assigned 1 point when present, yielding a theoretical score ranging from 0 to 6. In the present cohort, the observed scores ranged from 0 to 5 because no patient had all six components.

Patients were stratified into two groups according to their vascular burden score: low vascular burden (0–2) and high

vascular burden (3–5). This investigator-defined categorization was used to distinguish patients with fewer vascular risk factors and comorbidities from those with multiple concurrent vascular risk factors and established vascular comorbidities. The cutoff was not externally validated and should therefore not be interpreted as an established clinical threshold.

Data Collection

Demographic characteristics (age and sex), cardiovascular risk factors (smoking status, hypertension, diabetes mellitus, and hyperlipidemia), a history of coronary artery disease, and prior cerebrovascular events were retrieved from electronic medical records. Baseline laboratory parameters, including complete blood count, fasting glucose, glycated hemoglobin (HbA1c), renal function tests, and lipid profile, were obtained from blood samples collected before the CAS procedure.

PIV was calculated using peripheral blood cell counts according to the following formula:

PIV = (neutrophil count × platelet count × monocyte count) / lymphocyte count

PIV is considered a composite marker integrating circulating neutrophil, platelet, monocyte, and lymphocyte counts and has been investigated as a surrogate of systemic immune-inflammatory activity.

For regression analyses, PIV values were normalized by dividing by 100 (PIV100) to improve model interpretability.

The variables constituting the vascular burden score were considered components of the outcome and were therefore not entered as separate covariates in the multivariable regression models.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Akdeniz University (Approval No: TBAEK-510, Date: June 4, 2026). The requirement for informed consent was waived due to the retrospective nature of the study.

Statistical Analysis

Continuous variables were summarized as either mean ± standard deviation or median with interquartile range, depending on their distributions. Categorical variables were reported as counts and percentages. Comparisons between groups were conducted using the independent-samples t-test or Mann–Whitney U test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables when appropriate.

The association between PIV and the vascular burden score was evaluated using Spearman rank correlation analysis. Multivariable binary logistic regression analysis was performed to assess the independent association between PIV and high vascular burden. The model incorporated age, sex, and PIV100, and results were presented as odds ratios with corresponding 95% confidence intervals. Age and sex were included as basic demographic covariates, while PIV was the primary variable of interest. The individual components of the vascular burden score were not included in the model because they were used to define the dependent variable.

As a sensitivity analysis, the vascular burden score was also analyzed as an ordinal variable using ordinal logistic regression. The model was adjusted for age, sex, GFR, and PIV. The proportional odds assumption was assessed using the test of parallel lines. Receiver operating characteristic (ROC) curve analysis was performed to assess the discriminative ability of PIV in identifying high vascular burden. The optimal cutoff point was determined using the Youden index, and the area under the curve, along with sensitivity and specificity, was reported. A two-sided p value <0.05 was considered indicative of statistical significance. All analyses were carried out using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 221 patients who underwent carotid artery stenting were included in the study. According to the vascular burden score classification, 131 patients (59.3%) were categorized as having low vascular burden (score 0–2), whereas 90 patients (40.7%) were classified as having high vascular burden (score 3–5). Baseline demographic, clinical, laboratory, and echocardiographic characteristics according to vascular burden groups are summarized in Table 1. There were no significant differences between groups regarding age or sex distribution. The prevalence of diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and prior cerebrovascular events was higher in the high vascular burden group; these variables were components of the vascular burden score and therefore these differences were inherent in the score definition rather than independent findings. Smoking prevalence did not differ significantly between the groups (p = 0.145). Patients with high vascular burden had significantly higher fasting glucose and HbA1c levels (both p < 0.001) and a significantly lower ejection fraction (p = 0.003). Among hematological parameters, platelet count was significantly lower in patients with high vascular burden (254,717 ± 71,006 vs. 229,166 ± 56,602 cells/μL, p = 0.003). Neutrophil, lymphocyte, and monocyte counts did not differ significantly between the low- and high vascular burden groups (p = 0.317, p = 0.973, and p = 0.679, respectively). Despite the lower platelet count, PIV was significantly higher in patients with high vascular burden than in those with low vascular burden (median [IQR]: 428.9 [287.1–701.9] vs. 287.1 [202.1–452.5], p = 0.001) (Table 1).

Spearman correlation analysis demonstrated a positive but modest correlation between PIV and the vascular burden score (Spearman's rho = 0.317, p <0.001) (Table 2). In multivariable logistic regression analysis including age, sex, and PIV100, PIV100 remained independently associated with high vascular burden (OR: 1.152 per 100-unit increase, 95% CI: 1.058–1.255, p = 0.001), whereas age and sex were not independently associated with high vascular burden after adjustment (Table 3). In a sensitivity analysis using the vascular burden score as an ordinal variable, PIV remained independently associated with higher vascular burden. After adjustment for age, sex, and GFR, each 100-unit increase in PIV was associated with 11.6%

Table 1. Baseline demographic, clinical, laboratory, and echocardiographic characteristics according to vascular burden groups

Variable	Low vascular burden (0–2) (n=131)	High vascular burden (3–5) (n=90)	p-value
Age, years	69.4 ± 10.5	68.9 ± 9.5	0.719
Male sex, n (%)	101 (77.1)	73 (81.1)	0.474
Diabetes mellitus, n (%)	12 (9.2)	60 (66.7)	<0.001
Hypertension, n (%)	65 (49.6)	78 (86.7)	<0.001
Hyperlipidemia, n (%)	11 (8.4)	53 (58.9)	<0.001
Smoking, n (%)	28 (21.4)	27 (30.0)	0.145
A history of coronary artery disease, n (%)	12 (9.2)	29 (32.2)	<0.001
A history of cerebrovascular event, n (%)	68 (51.9)	65 (72.2)	0.002
GFR, mL/min/1.73m²	77 ± 20	75 ± 19	0.666
WBC, cells/μL	8135 ± 2285	8475 ± 2611	0.307
Neutrophil count, cells/μL†	5,200 (3,800–6,700)	4,800 (4,000–5,800)	0.317
Lymphocyte count, cells/μL†	2,000 (1,500–2,600)	2,100 (1,500–2,600)	0.973
Monocyte count, cells/μL†	600 (500–800)	600 (500–750)	0.679
Hemoglobin, g/dL	13.21 ± 1.69	13.31 ± 1.59	0.665
Platelet count, cells/μL	254,717 ± 71,006	229,166 ± 56,602	0.003
LDL cholesterol, mg/dL	117.08 ± 36.97	124.74 ± 38.61	0.138
HDL cholesterol, mg/dL	42.34 ± 9.14	40.82 ± 8.69	0.212
Total cholesterol, mg/dL	190.9 ± 42.8	200.2 ± 49.7	0.152
Triglycerides, mg/dL†	143 (108–191)	166 (118–238)	0.568
Creatinine, mg/dL	1.03 ± 0.30	1.10 ± 0.82	0.436
Sodium, mmol/L	137 ± 11	138 ± 3.2	0.484
Potassium, mmol/L	4.44 ± 0.4	4.51 ± 0.5	0.241
Glucose, mg/dL†	98 (90–122)	136 (108–175)	<0.001
HbA1c, %	6.14 ± 0.89	8.14 ± 2.04	<0.001
AST, U/L	22.5 ± 10.9	22.2 ± 9.3	0.863
ALT, U/L	19.4 ± 12.4	19.7 ± 12.0	0.835
Ejection fraction, %	61.9 ± 6.9	58.5 ± 9.2	0.003
PIV†	287.1 (202.1–452.5)	428.9 (287.1–701.9)	0.001

Values are presented as mean ± standard deviation (SD), median (interquartile range [IQR]), or number (percentage), as appropriate. Continuous variables were compared using the independent-samples t-test or Mann–Whitney U test according to data distribution, and categorical variables were compared using the chi-square test. †Variables with non-normal distribution are presented as median (IQR). Abbreviations: PIV, Pan-Immune-Inflammation Value; GFR, glomerular filtration rate; WBC, white blood cell count; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c, glycated hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Table 2. Correlation between Pan-Immune-Inflammation Value (PIV) and the vascular burden score

Variable	Spearman rho	p
PIV vs vascular burden score	0.317	<0.001

Spearman rank correlation analysis was used to evaluate the association between PIV and the vascular burden score. PIV: Pan-Immune-Inflammation Value.

Table 3. Multivariable logistic regression analysis identifying independent predictors of high vascular burden

Variable	OR	95% CI	p
Male sex	0.929	0.464–1.858	0.834
Age	0.997	0.970–1.025	0.855
PIV100	1.152	1.058–1.255	0.001

Multivariable logistic regression model adjusted for age, sex, and PIV100. PIV100 represents the Pan-Immune-Inflammation Value per 100-unit increase. OR, odds ratio; CI, confidence interval.

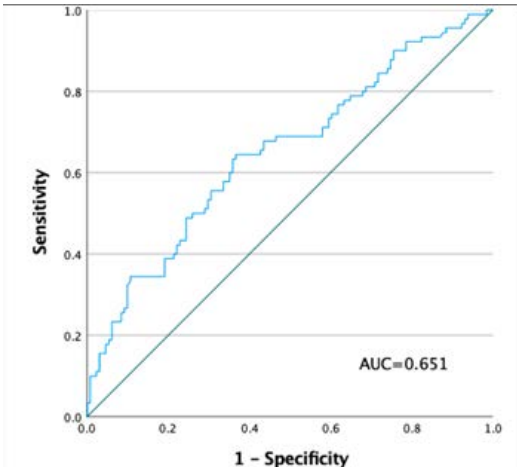

Figure 1. Receiver operating characteristic (ROC) curve of PIV for predicting high vascular burden.
The area under the curve (AUC) was 0.651 (95% CI: 0.577–0.725; p <0.001). The optimal cutoff value was 334, with 64% sensitivity and 60% specificity.

Table 4. Receiver operating characteristic (ROC) curve analysis of PIV for identifying high vascular burden

Parameter	Value
AUC	0.651
95% CI	0.577–0.725
p-value	<0.001
Optimal cutoff value	334
Sensitivity	64%
Specificity	60%

ROC curve analysis was performed to evaluate the discriminatory ability of PIV for identifying patients with high vascular burden. The optimal cutoff value was determined using the Youden index. AUC, area under the curve; CI, confidence interval.

higher odds of being in a higher vascular burden category (OR, 1.116; 95% CI, 1.062–1.174; p<0.001). The proportional odds assumption was not violated (test of parallel lines, p=0.181).

ROC curve analysis demonstrated modest discriminatory performance of PIV for identifying patients with high vascular burden (AUC = 0.651, 95% CI: 0.577–0.725, p <0.001). A PIV cutoff value of approximately 334 yielded a sensitivity of 64% and a specificity of 60% (Table 4, Figure 1).

DISCUSSION

In the present study, we found that higher PIV was independently associated with greater cumulative vascular comorbidity burden in patients undergoing CAS. Patients with higher vascular burden scores had significantly higher PIV levels, while ROC analysis showed only modest discriminatory performance. These findings suggest that PIV may reflect systemic inflammatory activity in patients with a greater accumulation of vascular risk factors and established vascular comorbidities. However, the observational design does not establish causality or prognostic utility. Atherosclerosis is increasingly recognized as a chronic inflammatory and immune-mediated disease characterized by endothelial dysfunction, lipid accumulation, leukocyte recruitment, platelet activation, and complex interactions between innate and adaptive immune responses. Persistent inflammation contributes to plaque progression, destabilization, and thromboembolic complications and represents an important component of residual cardiovascular risk. These mechanisms provide a biological rationale for investigating routinely available inflammatory biomarkers as potential indicators of systemic vascular disease burden (6–9,23).

Inflammatory activation is particularly relevant in patients undergoing CAS. Previous studies have demonstrated associations between inflammatory markers and peri-procedural embolization, stroke, restenosis, and adverse outcomes after carotid interventions. Aronow et al. demonstrated that leukocyte count independently predicted microembolic Doppler signals during carotid stenting, suggesting a relationship between systemic inflammatory activation and procedural embolization (24). Similarly, Gröschel et al. reported that preprocedural C-reactive protein levels were associated with stroke and death in patients undergoing carotid stenting (25). Wasser et al. further demonstrated an association between inflammatory markers and in-stent restenosis after CAS (26). Together, these findings indicate that systemic inflammatory activity is relevant to both the procedural and longer-term manifestations of carotid atherosclerotic disease.

Recent research has increasingly focused on composite inflammatory indices derived from routinely available hematological parameters. Such indices may capture the interaction between innate immune activation, platelet-mediated thrombosis, and lymphocyte-related immune regulation more comprehensively than individual inflammatory cell counts. PIV integrates neutrophil, platelet, monocyte, and lymphocyte counts into a single index and therefore theoretically captures several components of the systemic thromboinflammatory response simultaneously. The increasing use of composite immune-inflammatory biomarkers across cardiovascular diseases further supports their potential relevance for characterizing systemic vascular inflammation (17–19). Current evidence regarding composite immune-inflammatory biomarkers in cardiovascular disease is rapidly expanding. Previous studies have demonstrated associations between systemic immune-inflammatory indices and adverse cardiovascular outcomes in patients with cardiovascular disease. In the specific setting of carotid artery stenting, Morikawa et al. demonstrated that the systemic immune-inflammation index was associated with prognosis after CAS, further supporting the relevance of systemic inflammatory status in this population (27). The clinical relevance of composite immune-inflammatory indices has also been explored beyond carotid artery disease. Recent studies have evaluated nutritional and immune-inflammatory indices in patients with heart failure with preserved ejection fraction and those undergoing mitral balloon valvuloplasty, demonstrating their potential association with cardiovascular disease characteristics and outcomes (21,22). Although these studies evaluated different populations and inflammatory indices rather than PIV specifically, they provide additional evidence that readily available composite inflammatory markers may reflect the broader systemic burden of cardiovascular disease.

Our findings extend this concept to patients undergoing CAS by examining the relationship between PIV and cumulative vascular comorbidity burden rather than procedural outcomes or anatomical carotid disease severity. The vascular burden score used in the present study comprised six components: hypertension, diabetes mellitus, hyperlipidemia, smoking, a history of coronary artery disease, and previous cerebrovascular events, with one point assigned for each component. Thus, the score should be interpreted as an investigator-defined measure of the accumulation of major vascular risk factors and established vascular comorbidities, rather than as an anatomical measure of carotid stenosis, plaque burden, or total vascular lesion extent. Patients with higher scores had significantly higher PIV values, supporting an association between systemic inflammatory activity and the accumulation

of vascular comorbidities. Importantly, the higher prevalence of diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and previous cerebrovascular events in the high-burden group should not be interpreted as independent findings, because these variables were themselves components of the vascular burden score. Their greater frequency in the high-score group was therefore expected by definition. Instead, the more relevant findings were the differences in variables that were not directly incorporated into the score, particularly fasting glucose, HbA1c, ejection fraction, platelet count, and PIV.

PIV remained independently associated with high vascular burden after adjustment for age and sex. Each 100-unit increase in PIV was associated with approximately 15% higher odds of belonging to the high vascular burden group. Importantly, this association remained consistent when the vascular burden score was analyzed across its full ordinal range rather than dichotomized. In the ordinal logistic regression model, each 100-unit increase in PIV was associated with 11.6% higher odds of being in a higher vascular burden category (OR, 1.116; 95% CI, 1.062–1.174; $p<0.001$), after adjustment for age, sex, and GFR. The proportional odds assumption was not rejected (test of parallel lines, $p=0.181$), supporting the validity of the ordinal model. These findings provide additional support for the robustness of the association between PIV and cumulative vascular comorbidity burden. The absence of an independent association between age and vascular burden should be interpreted cautiously, particularly given the cross-sectional design and relatively limited sample size, and should not be interpreted as evidence that inflammatory activity reflects vascular aging more accurately than chronological age. The correlation between PIV and the vascular burden score was positive but modest (Spearman's rho = 0.317), indicating that the association between PIV and cumulative vascular comorbidity burden was relatively limited. Furthermore, the absence of adjustment for all potential inflammatory and clinical confounders means that residual confounding cannot be excluded. Therefore, the present findings support an independent statistical association between PIV and cumulative vascular comorbidity burden but do not establish PIV as a causal determinant or validated clinical predictor.

The ROC analysis further emphasizes the need for a cautious interpretation. PIV demonstrated an AUC of 0.651, with a sensitivity of 64% and specificity of 60% at a cutoff of approximately 334. These values indicate only modest discriminatory ability and are insufficient to support the use of PIV as a standalone diagnostic or risk-stratification tool. Rather, PIV may be considered a complementary inflammatory marker that could potentially provide additional information when interpreted together with established clinical risk factors and vascular imaging findings. Whether PIV provides incremental predictive value beyond conventional clinical and imaging variables remains unknown and requires prospective validation. The significantly lower platelet count observed in the high vascular burden group despite higher PIV values deserves consideration. PIV is a composite index determined by the combined values of neutrophil, platelet, monocyte, and lymphocyte counts rather than by platelet count alone. In the present study, neutrophil, lymphocyte, and monocyte counts did not differ significantly between the low- and high vascular burden groups ($p=0.317$, $p=0.973$, and $p=0.679$, respectively). Therefore, the higher PIV observed in the high-burden group cannot be attributed to a significant difference in any single PIV component based on these univariate comparisons. Rather, the finding reflects the combined contribution of the four cellular parameters to the composite PIV. Nevertheless, because PIV is a multiplicative index, the relative contribution of each individual component to the observed between-group difference cannot be determined from these analyses alone.

Diabetes mellitus was more prevalent in patients with high vascular burden, who also had significantly higher fasting glucose and HbA1c levels. Diabetes contributes to accelerated atherosclerosis through chronic low-grade inflammation, endothelial dysfunction, oxidative stress, and platelet activation (28,29). However, because diabetes was one of the six components of the vascular burden score, its higher prevalence in the high-burden group was inherent in the score construction rather than an independent finding. The observed metabolic differences nevertheless provide biological context for the association between systemic inflammatory activity and cumulative vascular comorbidity burden. Another important consideration is the potential influence of recent cerebrovascular events on PIV. Because the study was retrospective, the exact interval between a previous cerebrovascular event and blood sampling could not be consistently standardized. Consequently, acute or subacute inflammatory responses related to a recent cerebrovascular event may have contributed to PIV values in some patients. This issue is particularly relevant because previous cerebrovascular events were also incorporated into the vascular burden score. Therefore, the association between PIV and the composite score may partly reflect inflammation associated with recent vascular events rather than solely chronic systemic inflammatory burden. The present study has several strengths. First, to our knowledge, few studies have specifically examined the association between PIV and cumulative vascular comorbidity burden in patients undergoing CAS. Second, PIV is derived from routinely available complete blood count parameters and therefore does not require specialized or costly laboratory testing. Third, the study explicitly distinguishes cumulative vascular comorbidity burden from anatomical carotid disease burden, thereby addressing a clinically relevant aspect of systemic atherosclerotic disease that may not be captured by stenosis severity alone.

Study Limitations

Several limitations should be acknowledged. First, the retrospective, single-center design and relatively modest sample size limit causal inference, precision of estimates, and generalizability. Second, the vascular burden score was investigator-defined and has not been externally validated; therefore, it should be considered a descriptive measure of cumulative vascular comorbidity burden rather than a

validated risk score. Third, the absence of longitudinal follow-up precluded assessment of the prognostic value of PIV for subsequent clinical events. Fourth, detailed information on symptomatic status, carotid stenosis characteristics, plaque morphology, and background medical treatment was not consistently available. Finally, potential confounding factors, including active infection, chronic inflammatory conditions, and medications affecting inflammatory or hematological parameters, could not be comprehensively assessed, and advanced inflammatory biomarkers such as high-sensitivity C-reactive protein and interleukin-6 were not routinely available.

Future prospective multicenter studies with larger samples, standardized blood sampling, detailed carotid imaging, and longitudinal clinical follow-up are warranted to determine whether PIV provides incremental prognostic or risk-stratification value beyond conventional clinical and imaging variables.

CONCLUSION

In patients undergoing carotid artery stenting, higher PIV was independently associated with greater cumulative vascular comorbidity burden. However, its modest discriminatory performance does not support its use as a standalone risk-stratification or prognostic tool. PIV may provide complementary information regarding systemic immune-inflammatory activity in this population. Further prospective studies are needed to establish its clinical utility.

DECLARATIONS

Conflict of Interest: *The authors declare that they have no conflicts of interest.*

Financial Disclosure: *This study received no specific financial support from any public, commercial, or non-profit funding agency.*

Acknowledgements: *N.A.*

Funding: *No financial support was received for this study.*

Author Contributions: *Concept: T.K., A.Ü.K., Ö.K. Design: T.K., A.Ü.K. Data Collection or Processing: T.K., A.Ü.K., Ö.K. Analysis or Interpretation: A.Ü.K. Literature Search: T.K. Writing: T.K.*

Address correspondence to: *Aysegul Ulgen Kunak, University of Health Sciences, Antalya Training and Research Hospital, Department of Cardiology, Antalya, Türkiye*
e-mail: *aysegululgen@yahoo.com*

REFERENCES

1. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2021;20(10):795-20. doi: 10.1016/S1474-4422(21)00252-0. Epub 2021 Sep 3.
2. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation. 2023;147(8):e93-e621. doi: 10.1161/CIR.0000000000001123. Epub 2023 Jan 25.
3. Brott TG, Hobson RW 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010;363(1):11-23. doi: 10.1056/NEJMoa0912321. Epub 2010 May 26. Erratum in: N Engl J Med. 2010;363(2):198; 363(5):498.
4. Bonati LH, Kakkos S, Berkefeld J, et al. European Stroke Organisation guideline on endarterectomy and stenting for carotid artery stenosis. Eur Stroke J. 2021;6(2):I-XLVII. doi: 10.1177/23969873211012121. Epub 2021 May 11.
5. Naylor AR. Why is the management of asymptomatic carotid disease so controversial? Surgeon. 2015;13(1):34-43. doi: 10.1016/j.surge.2014.08.004. Epub 2014 Oct 14.
6. Libby P, Loscalzo J, Ridker PM, et al. Inflammation, immunity, and infection in atherothrombosis: JACC review topic of the week. J Am Coll Cardiol. 2018;72(17):2071-81. doi: 10.1016/j.jacc.2018.08.1043.
7. Libby P. The changing landscape of atherosclerosis. Nature. 2021;592(7855):524-33. doi: 10.1038/s41586-021-03392-8. Epub 2021 Apr 21.
8. Hansson GK, Libby P, Tabas I. Inflammation and plaque vulnerability. J Intern Med. 2015;278(5):483-93. doi: 10.1111/joim.12406. Epub 2015 Aug 11.
9. Bäck M, Yurdagul A Jr, Tabas I, et al. Inflammation and its resolution in atherosclerosis: mediators and therapeutic opportunities. Nat Rev Cardiol. 2019;16(7):389-06. doi: 10.1038/s41569-019-0169-2.
10. Saba L, Saam T, Jäger HR, et al. Imaging biomarkers of vulnerable carotid plaques for stroke risk prediction and their potential clinical implications. Lancet Neurol. 2019;18(6):559-572. doi: 10.1016/S1474-4422(19)30035-3. Epub 2019 Apr 4.
11. Koupenova M, Clancy L, Corkrey HA, Freedman JE. Circulating platelets as mediators of immunity, inflammation, and thrombosis. Circ Res. 2018;122(2):337-351. doi: 10.1161/CIRCRESAHA.117.310795.
12. Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med. 2017;377(12):1119-31. doi: 10.1056/NEJMoa1707914. Epub 2017 Aug 27.
13. Subramanian A, Delaney S, Murphy SJX, et al. Platelet biomarkers in patients with atherosclerotic extracranial carotid artery stenosis: a systematic review. Eur J Vasc Endovasc Surg. 2022;63(3):379-89. doi: 10.1016/j.ejvs.2021.10.045. Epub 2022 Feb 15.
14. Jackson SP, Darbousset R, Schoenwaelder SM. Thromboinflammation: challenges of therapeutically targeting coagulation and other host defense mechanisms. Blood. 2019;133(9):906-18. doi: 10.1182/blood-2018-11-882993. Epub 2019 Jan 14.
15. von Hundelshausen P, Weber C. Platelets as immune cells: bridging inflammation and cardiovascular disease. Circ Res. 2007;100(1):27-40. doi: 10.1161/01.RES.0000252802.25497.b7.
16. Nording HM, Seizer P, Langer HF. Platelets in inflammation and atherogenesis. Front Immunol. 2015;6:98. doi: 10.3389/fimmu.2015.00098.
17. Bradley NA, Roxburgh CSD, McMillan DC, Guthrie GJK. A systematic review of the role of systemic inflammation-based prognostic scores in patients with abdominal aortic aneurysm. Surgeon. 2025;23(1):e1-e8. doi: 10.1016/j.surge.2024.08.014. Epub 2024 Aug 26.
18. Zhang L, Lyu Q, Zhou W, et al. High systemic immune-inflammation index is associated with carotid plaque vulnerability: new

findings based on carotid ultrasound imaging in patients with acute ischemic stroke. Front Neurol. 2022;13:959531. doi: 10.3389/fneur.2022.959531.
19. Antonopoulos AS, Angelopoulos A, Papanikolaou P, et al. Biomarkers of vascular inflammation for cardiovascular risk prognostication: a meta-analysis. JACC Cardiovasc Imaging. 2022;15(3):460-71. doi: 10.1016/j.jcmg.2021.09.014. Epub 2021 Nov 17.
20. Keskin M, Öcal L, Cerşit S, et al. The predictive role of a novel risk index in patients undergoing carotid artery stenting: systemic immune-inflammation index. J Stroke Cerebrovasc Dis. 2021;30(9):105955. doi: 10.1016/j.jstrokecerebrovasdis.2021.105955.
21. Yavuz YE, Tatar S, Şahin AT, et al. Predictive role of nutritional and immune-inflammatory indexes in the diagnostic work-up and risk stratification of heart failure with preserved ejection fraction. Minerva Cardiol Angiol. 2025 Jun 27. doi: 10.23736/S2724-5683.25.06817-6.
22. Aydın, N, Tatar, S, Şahin, AT, et al. Does the systemic immune inflammation index and plasma atherogenic index predict poor prognosis in patients undergoing mitral balloon valvuloplasty?. Gazi Medical Journal, 2024;35(3), 310.
23. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227-37. doi: 10.1093/eurheartj/ehab484. Erratum in: Eur Heart J. 2022;43(42):4468.
24. Aronow HD, Shishehbor M, Davis DA, et al. Leukocyte count predicts microembolic Doppler signals during carotid stenting: a link between inflammation and embolization. Stroke. 2005;36(9):1910-14. doi: 10.1161/01.STR.0000177610.33478.65.
25. Gröschel K, Ernemann U, Larsen J, et al. Preprocedural C-reactive protein levels predict stroke and death in patients undergoing carotid stenting. AJNR Am J Neuroradiol. 2007;28(9):1743-46. doi: 10.3174/ajnr.A0650.
26. Wasser K, Schnaudigel S, Wohlfahrt J, et al. Inflammation and in-stent restenosis: the role of serum markers and stent characteristics in carotid artery stenting. PLoS One. 2011;6(7):e22683. doi: 10.1371/journal.pone.0022683.
27. Morikawa S, Okumura K, Inoue N, et al. Systemic immune-inflammation index as a predictor of prognosis after carotid artery stenting compared with C-reactive protein. PLoS One. 2023;18(7):e0288564. doi: 10.1371/journal.pone.0288564.
28. American Diabetes Association Professional Practice Committee. Cardiovascular disease and risk management: standards of care in diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S179-S218. doi: 10.2337/dc24-S010.
29. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases. Eur Heart J. 2020;41(2):255-23. doi: 10.1093/eurheartj/ehz486.