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RESEARCH ARTICLE

Evaluation of pentraxin-3 levels as a biomarker of large vessel occlusion in ischemic stroke

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ABSTRACT

Objective: Early diagnosis of acute ischemic stroke patients with large vessel occlusion (LVO) and the transfer of patients who require endovascular treatment to specialized stroke centers are critical for patients. Pentraxin-3 (PTX-3) is a biomarker of vascular inflammation, and its role in stroke, including its relationship with clinical features, is being investigated. In this study, we evaluated the value of PTX-3 levels in the diagnosis of LVO and their relationship with clinical features.

Methods: This study included retrospectively and prospectively enrolled patients diagnosed with acute ischemic stroke. Patients were divided into two groups according to imaging findings: those with and those without LVO. Serum PTX-3 levels were measured and compared between the groups. Stroke severity was evaluated at admission using the National Institutes of Health Stroke Scale (NIHSS), and clinical outcome was evaluated at the 90th day using the modified Rankin Scale (mRS). Correlation, ROC analysis, and logistic regression methods were used in statistical analyses.

Results: Data from 81 patients were analyzed. Although PTX-3 levels were higher in patients with LVO, the difference was not statistically significant. The discriminative power of PTX-3 for LVO was limited (AUC = 0.58). A positive correlation was found between PTX-3 levels and admission NIHSS. Although an association between PTX-3 and poor clinical outcome was observed in univariate analyses, PTX-3 was not an independent marker in multivariable analyses. The addition of PTX-3 to clinical models did not increase predictive power.

Conclusion: In patients with acute ischemic stroke with LVO, PTX-3 was not a sufficient biomarker for confirming the diagnosis. Although PTX-3 was associated with stroke severity, it could not predict clinical outcome independently. Based on the current findings, PTX-3 does not appear to have a clear contribution to the clinical decision-making process.

Keywords: acute ischemic stroke, clinical outcome, large vessel occlusion, pentraxin-3

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INTRODUCTION

Ischemic stroke, which poses a significant burden to public health, has entered a new era in treatment since the effectiveness of endovascular thrombectomy was demonstrated in 2015. The demonstrated effectiveness of stroke treatments, together with the recognition that this effect is time-dependent, has revealed that neuronal loss continues with every minute lost (1,2). Therefore, many countries worldwide are establishing centers dedicated to stroke treatment according to existing healthcare resources and are developing organizational schemes aimed at shortening the time to reach these centers and inter-center transfer durations.

Stroke centers are comprehensive units where both intravenous thrombolytic (IVT) and endovascular treatment (EVT) can be performed. These treatments are applied to patients with large vessel occlusion (LVO), and the success of the treatment is time-dependent. Therefore, it is important that patients with suspected ischemic stroke are rapidly evaluated and transferred to comprehensive centers. Especially in rural areas where advanced imaging methods such as CT and MR are not available, supporting the diagnosis with a measurable blood biomarker is essential. However, to date, a reliable biomarker that can predict LVO has not been identified (3).

Inflammatory markers begin to be produced in the occluded or hypoperfused vessel and brain tissue after acute ischemic stroke (4). Pentraxin-3 (PTX-3) is a member of the long pentraxin family (5). Although classical acute phase reactants are produced by the liver, the PTX-3 molecule is produced in various cells such as endothelial cells, macrophages, dendritic cells, and vascular smooth muscle cells (6). In an animal study, PTX-3 was demonstrated to support cerebral blood flow, angiogenesis, and neuronal viability (7). Although it has been identified as a neuroprotective molecule in animal experiments, whether it is associated with prognosis in patients with ischemic stroke has not been fully established. In a study conducted in stroke patients, Pentraxin-3 levels were reported to be associated with poor prognosis in minor strokes on the basis of large vessel atherosclerosis (8,9), whereas another study found no association with prognosis (10). In the literature, no study evaluating the relationship between the presence of LVO and PTX-3 levels in patients with ischemic stroke has been identified.

In patients with ischemic stroke and LVO, early recognition for EVT and rapid transfer to appropriate centers are necessary. In this context, the identification of a blood-measurable biomarker may offer new opportunities for clinical practice, especially in patient groups where advanced imaging modalities are not available or imaging cannot be performed. In this study, we aimed to evaluate the relationship between PTX-3 levels by comparing patients with and without LVO. As a secondary outcome, we planned to evaluate its association with the clinical outcomes of the patients.

MATERIALS AND METHODS

This study was designed with both retrospective and prospective components. Patients who had blood samples collected within the scope of the thesis study titled "Comparison of Matrix Metalloproteinase-28 Levels According to Etiology in Patients with Ischemic Stroke," conducted between June 2024 and October 2025, and who met the inclusion and exclusion criteria of the present study were included. If the target sample size was not reached, patients who presented to our clinic until January 2026 and met the study criteria were prospectively enrolled to complete the sample.

We obtained general medical histories of patients admitted to our hospital with acute ischemic stroke and performed neurological examinations. We recorded age, sex, admission examination findings, vascular risk factors, and post-stroke echocardiography (ECHO) and electrocardiography (ECG) findings of the cases. The presence of LVO in patients was recorded. The treatments applied to the patients were recorded. Blood tests were obtained before administration if reperfusion therapy (EVT or IVT) was to be given. Stroke severity was assessed at admission using the National Institutes of Health Stroke Scale (NIHSS). Clinical outcome was evaluated at the third month using the modified Rankin Scale (mRS).

Patients who met the study criteria were divided into two groups according to imaging findings: patients

with occlusion of the internal carotid artery (ICA) or the M1 segment of the middle cerebral artery (MCA) were classified as the large vessel occlusion group; patients without occlusion in these segments were classified as the control group.

Hemogram, ferritin, C-reactive protein (CRP), troponin I or T, urea, creatinine, low-density lipoprotein (LDL), and triglyceride levels obtained at emergency department admission were evaluated. Blood samples for PTX-3 were obtained at the time of admission to the emergency department. The samples were kept at room temperature for 2 hours and then centrifuged at 1000 rpm for 10 minutes to obtain serum, which was stored at −80°C. At the end of the study period, the samples were analyzed in the biochemistry laboratory using the A.B.T. Human PTX-3/TGS-14 (Pentraxin 3) ELISA kit (Cat. No# ABT3185Hu, Atlas Biotechnology, Ankara, Turkey).

Statistical analysis

Distribution of continuous variables was assessed with the Shapiro–Wilk test and graphical inspection. Normally distributed continuous variables were reported as mean ± standard deviation and compared with the Student's t-test (or Welch's t-test when variance homogeneity, assessed by Levene's test, was doubtful); non-normally distributed continuous and ordinal variables were reported as median with interquartile range and compared with the Mann–Whitney U test. Categorical variables were compared with the Pearson χ^2 test or Fisher's exact test, as appropriate. Spearman's rank correlation coefficient was used to examine the association between serum PTX-3 and clinical and laboratory variables; 95% confidence intervals were derived by the Fisher z transformation. Discriminative performance of PTX-3 for each endpoint was quantified by the receiver-operating-characteristic area under the curve with bootstrap percentile 95% confidence intervals (2,000 resamples), and the Youden index was used to identify an optimal cut-off. Independent predictors of each endpoint were modeled by binary logistic regression. A parsimonious multivariable model was pre-specified for each endpoint, with predictors chosen for clinical relevance (primary exposure and core risk factors) rather than data-driven selection; variance-inflation factors, the Hosmer–Lemeshow goodness-of-fit test, and Nagelkerke's R^2 are reported. Sensitivity analyses (log transformation, Winsorization, outlier exclusion, median imputation, and sex- and age-stratified re-analysis) were pre-specified to probe the robustness of the primary inference. Two-sided $\alpha = .05$ was used throughout. Analyses were conducted in Python 3.11 with pandas 2.2, scipy 1.13, statsmodels 0.14, and scikit-learn 1.5.

RESULTS

Sample characteristics and between-group comparisons

The analysis sample comprised 81 patients with acute anterior-circulation ischemic stroke presenting within 24 hours of symptom onset: 40 patients with large-vessel occlusion (LVO+; internal carotid artery and/or middle-cerebral-artery M1 segment) and 41 without (LVO−). Baseline demographic, clinical, and laboratory characteristics are presented in Table 1. The groups were comparable in age (M = 68.6, SD = 13.0 years in LVO+ vs. M = 68.2, SD = 12.7 years in LVO−; p = .647) and in sex distribution (47.5% vs. 39.0% female; p = .585). Patients with LVO presented with substantially greater neurological deficit than those without, as indicated by a median NIHSS score on admission of 14 (IQR = 10–20) versus 4 (IQR = 2–6; p < .001; rank-biserial r = −0.79) and by a median baseline mRS of 5 (IQR = 4–5) versus 1 (IQR = 1–3; p < .001). Atrial fibrillation (AF) was markedly more prevalent in LVO+ patients than in LVO− patients, both on admission electrocardiography (60.0% vs. 7.3%; p < .001, $\phi = .53$) and on the composite ECG-or-Holter indicator (65.0% vs. 22.0%; p < .001, $\phi = .41$). Routine hematological and biochemical parameters — including hemoglobin, C-reactive protein, ferritin, troponin I, urea, and creatinine — did not differ between the groups (all p ≥ .34). Unfavorable 90-day functional outcome (mRS > 2) occurred in 62.5% of LVO+ patients compared with 7.3% of LVO− patients (p < .001, $\phi = .55$).

Serum pentraxin-3 concentrations by LVO status

Admission serum PTX-3 concentrations were compatible with a normal distribution in both groups (Shapiro–Wilk W = 0.98, p = .747 in LVO+; W = 0.95,

Table 1. Baseline demographic, clinical, and laboratory characteristics of the study groups

Variable	Total (N = 81)	LVO+ (n = 40)	LVO− (n = 41)	Test statistic	p
Age, years, Mdn (IQR)	69 (61–78)	69 (63–79)	68 (59–78)	U = 869.0	.647
Female sex, n (%)	35 (43.2)	19 (47.5)	16 (39.0)	$\chi^2(1) = 0.30$	.585
AF on admission ECG, n (%)	27 (33.3)	24 (60.0)	3 (7.3)	$\chi^2(1) = 22.97$	< .001
AF (ECG or Holter), n (%)	35 (43.2)	26 (65.0)	9 (22.0)	$\chi^2(1) = 13.59$	< .001
Holter-detected AF, n (%)	8 (9.9)	2 (5.0)	6 (14.6)	†	.264
Positive echo finding, n (%)	75 (96.2)	36 (92.3)	39 (100.0)	†	.240
NIHSS on admission, Mdn (IQR)	7 (4–16)	14 (10–20)	4 (2–6)	U = 1471.0	< .001
Baseline mRS, Mdn (IQR)	3 (1–5)	5 (4–5)	1 (1–3)	U = 1456.0	< .001
Hemoglobin, g/dL, M (SD)	12.97 (1.72)	12.80 (1.99)	13.13 (1.42)	t(79) = −0.87	.388
CRP, mg/dL, Mdn (IQR)	0.31 (0.17–0.64)	0.29 (0.15–0.75)	0.37 (0.21–0.57)	U = 748.0	.499
Ferritin, ng/mL, Mdn (IQR)	73.7 (48.2–155.0)	72.6 (39.4–155.0)	82.8 (54.2–208.0)	U = 524.5	.361
Troponin I, ng/L, Mdn (IQR)	8.4 (4.0–14.9)	9.0 (5.3–15.5)	7.6 (3.3–13.9)	U = 880.0	.340
Urea, mg/dL, Mdn (IQR)	35.3 (26.5–51.0)	36.1 (26.2–55.0)	36.4 (27.0–50.0)	U = 895.0	.402
Creatinine, mg/dL, Mdn (IQR)	0.94 (0.74–1.08)	0.89 (0.70–1.12)	0.90 (0.77–1.05)	U = 843.5	.608
Serum PTX-3, pg/mL, M (SD)	337.2 (141.7)	355.6 (137.1)	319.2 (145.5)	t(79) = 1.16	.249
90-day mRS, Mdn (IQR)	1 (1–4)	4 (1.75–6)	1 (1–1)	U = 1335.0	< .001
Unfavourable outcome, n (%)	28 (34.6)	25 (62.5)	3 (7.3)	$\chi^2(1) = 24.87$	< .001

LVO = large vessel occlusion; M = mean; SD = standard deviation; Mdn = median; IQR = interquartile range (Q1–Q3); AF = atrial fibrillation; ECG = electrocardiogram; NIHSS = National Institutes of Health Stroke Scale; mRS = modified Rankin Scale; PTX-3 = pentraxin 3; CRP = C-reactive protein; U = Mann–Whitney U statistic; t = Student t statistic; χ^2 = Pearson chi-square statistic. Normally distributed continuous variables (hemoglobin, serum PTX-3; assessed by Shapiro–Wilk test within each group) were compared with the Student t test. Non-normally distributed continuous and ordinal variables were compared with the Mann–Whitney U test. Categorical variables were compared with the Pearson χ^2 test. † Fisher's exact test (expected cell count < 5). Denominators for percentages use the non-missing count per variable (range 78–81).

p = .054 in LVO−), and variance homogeneity was supported by Levene's test (F(1,79) = 0.12, p = .735). Mean serum PTX-3 was numerically higher in the LVO+ group (M = 355.64, SD = 137.09 pg/mL) than in the LVO− group (M = 319.16, SD = 145.46 pg/mL), but the between-group difference did not reach statistical significance (t(79)= 1.16, p = .249, Cohen's d = 0.26; 95% CI of mean difference [−26.00, 98.97] pg/mL). The distribution of PTX-3 values by group is illustrated in Figure 1. Welch's t-test produced an essentially identical result (t(78.91) = 1.16, p = .249), and a Mann–Whitney U test confirmed the non-significant pattern (U = 914.5, p = .378, rank-biserial r = 0.12; Hodges–Lehmann location shift = 25.2 pg/mL, bootstrap 95% CI [−45.1, 94.3]). The post-hoc power achieved for the observed effect size (d = 0.26) was approximately .21. Additional robustness checks (log transformation, Winsorization, outlier exclusion, and stratified re-analysis) uniformly confirmed the null finding.

Correlations of serum pentraxin-3 with clinical variables

Spearman rank-order correlations among serum PTX-3 and the principal clinical and laboratory variables are presented in Table 2. Serum PTX-3 was significantly and positively correlated with admission NIHSS (ρ = .29, 95% CI [.08, .48], p = .009), indicating that higher PTX-3 concentrations accompanied greater neurological deficit at presentation; the bivariate relationship is illustrated in Figure 2. Correlations of PTX-3 with age (ρ = .20, p = .077), baseline mRS (ρ = .20, p = .077), serum creatinine (ρ = .22, p = .055), and 90-day mRS (ρ = .18, p = .115) were of borderline significance and small in magnitude. Serum PTX-3 was

not significantly correlated with CRP (ρ = .17, p = .132), consistent with the view that the two acute-phase reactants reflect distinct biological compartments. As expected, admission NIHSS was strongly correlated with baseline mRS (ρ = .91, p < .001) and with 90-day mRS (ρ = .72, p < .001).

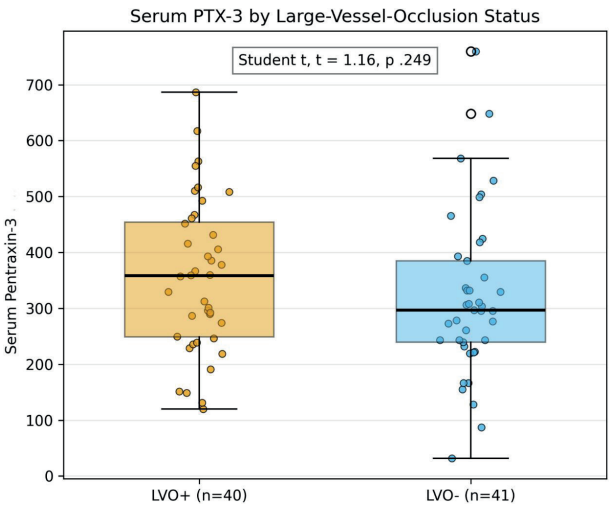

Figure 1. Serum pentraxin-3 concentrations in patients with and without large-vessel occlusion.

Box-and-whisker plot of admission serum PTX-3 in the LVO+ (n = 40) and LVO− (n = 41) groups. Boxes = interquartile range; horizontal line = median; whiskers = 1.5 × IQR; individual observations overlaid with lateral jitter. t(79) = 1.16, p = .249, Cohen's d = 0.26, 95% CI of mean difference [−26.00, 98.97] pg/mL.

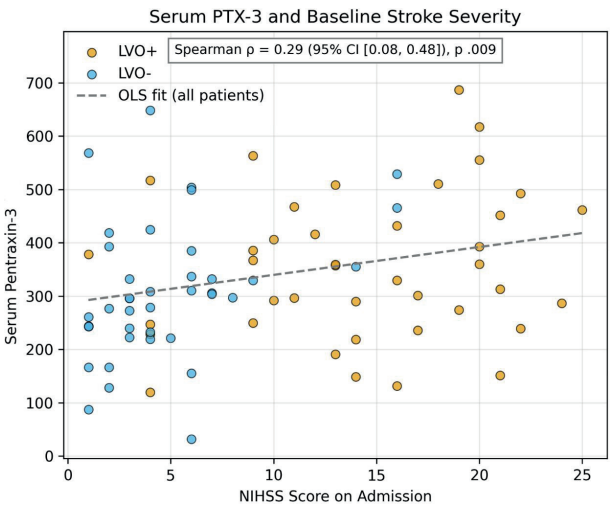

Figure 2. Scatter plot of serum pentraxin-3 against admission NIHSS, by LVO status.

Observations are colour-coded by LVO status. The dashed grey line is an ordinary-least-squares fit (visual reference only); the reported statistic is Spearman's ρ = .29, 95% CI [.08, .48], p = .009.

Table 2. Means, standard deviations, and spearman correlations among study variables

Variable	M	SD	1	2	3	4	5	6	7	8
1. Serum PTX-3 (pg/mL)	337.18	141.70	—							
2. NIHSS on admission	9.53	6.95	.29**	—						
3. Baseline mRS	2.98	1.60	.20	.91***	—					
4. 90-day mRS	2.49	1.94	.18	.72***	.81***	—				
5. Age (years)	68.40	12.76	.20	.17	.14	.27*	—			
6. CRP (mg/dL)	0.86	1.63	.17	.04	-.03	.06	.03	—		
7. Hemoglobin (g/dL)	12.97	1.72	-.08	-.13	-.12	-.18	-.43***	-.16	—	
8. Creatinine (mg/dL)	1.03	0.41	.22	.12	.09	.18	.07	.07	.03	—

N = 69–81 per correlation (pairwise deletion of missing values). M and SD are shown for all variables to facilitate comparison; note that CRP, creatinine, and NIHSS are non-normally distributed. Values in the lower triangle are Spearman's rank-order correlation coefficients (ρ). PTX-3 = pentraxin 3; NIHSS = National Institutes of Health Stroke Scale; mRS = modified Rankin Scale; CRP = C-reactive protein.

* p < .05. ** p < .01. *** p < .001.

Discriminative performance of serum pentraxin-3

The discriminative performance of serum PTX-3 and benchmark comparators is summarized in Table 3 and illustrated in Figure 3. For discrimination of large-vessel occlusion (Figure 3A), serum PTX-3 yielded an AUC of .58 (95% CI [.45, .71]); the Youden-optimal cut-off of 357 ng/mL provided a sensitivity of 52.5% and a specificity of 73.2%, with positive and negative predictive values of 65.6% and 61.2%. The 95% CI of the AUC crossed the chance-level value of 0.50. By contrast, admission NIHSS yielded an AUC of .90 (95% CI [.82, .96]). Adding PTX-3 to the full clinical model (age, sex, NIHSS, AF) did not improve discrimination (ΔAUC = +.001; LR $\chi^2(1) = 0.51$, p = .474). For 90-day unfavorable outcome (Figure 3B), PTX-3 produced an AUC of .66 (95% CI [.51, .79]), a value only marginally above the chance level of .50 at the lower confidence bound, indicating limited and statistically uncertain discriminative ability for this endpoint. Adding PTX-3 to the full clinical model (age, sex, NIHSS, LVO) similarly provided negligible incremental value (ΔAUC = +.003; LR $\chi^2(1) = 1.13$, p = .289).

Univariate and multivariable logistic regression for large-vessel occlusion

Univariate and prespecified hierarchical multivariable logistic-regression results for the LVO endpoint are presented in Table 4. In univariate analyses, the strongest predictors of LVO were admission NIHSS (OR = 1.39, 95% CI [1.22, 1.60], p < .001), baseline mRS (OR = 3.47, 95% CI [2.15, 5.59], p < .001), and atrial fibrillation (OR = 6.81, 95% CI [2.55, 18.19], p < .001). Serum PTX-3 was not significantly associated with LVO at the univariate level (OR = 1.002, 95% CI [0.999, 1.005], p = .248). Age, sex, and all laboratory markers were non-significant (all p ≥ .34).

Table 3. Receiver-operating-characteristic analysis: discriminative performance of single markers and clinical models for the two endpoints

Endpoint / Model	n	AUC [95% CI]	Sensitivity, %	Specificity, %	ΔAUC	LR $\chi^2(1)$, p
Large-vessel occlusion						
Serum PTX-3	81	.58 [.45, .71]	52.5	73.2	—	—
CRP	81	.46 [.33, .59]	—	—	—	—
NIHSS	81	.90 [.82, .96]	—	—	—	—
Clinical model [a]	81	.92 [.85, .97]	—	—	ref.	—
Clinical model + PTX-3	81	.92 [.85, .97]	—	—	+.001	0.51, .474
90-day unfavourable outcome						
Serum PTX-3	81	.66 [.51, .79]	60.7	71.7	—	—
NIHSS	81	.91 [.83, .97]	—	—	—	—
LVO status	81	.81 [.72, .89]	—	—	—	—
Clinical model [b]	81	.94 [.88, .99]	—	—	ref.	—
Clinical model + PTX-3	81	.95 [.89, .99]	—	—	+.003	1.13, .289

AUC = area under the receiver-operating-characteristic curve; CI = confidence interval; ΔAUC = change in AUC when PTX-3 is added to the clinical model; LR = likelihood-ratio test comparing the clinical model with vs. without PTX-3; PTX-3 = pentraxin 3; CRP = C-reactive protein; NIHSS = National Institutes of Health Stroke Scale; AF = atrial fibrillation; LVO = large-vessel occlusion. Sensitivity and specificity are reported at the Youden-optimal cut-off of 357 pg/mL for PTX-3 only (PPV = 65.6%, NPV = 61.2% for LVO; PPV = 53.1%, NPV = 77.6% for 90-day outcome). Composite-model AUCs were derived from the predicted probabilities of the corresponding logistic-regression equations. Bootstrap percentile CIs (2,000 replicates). [a] Clinical model for LVO: age, sex, NIHSS, and AF. [b] Clinical model for 90-day outcome: age, sex, NIHSS, and LVO status.

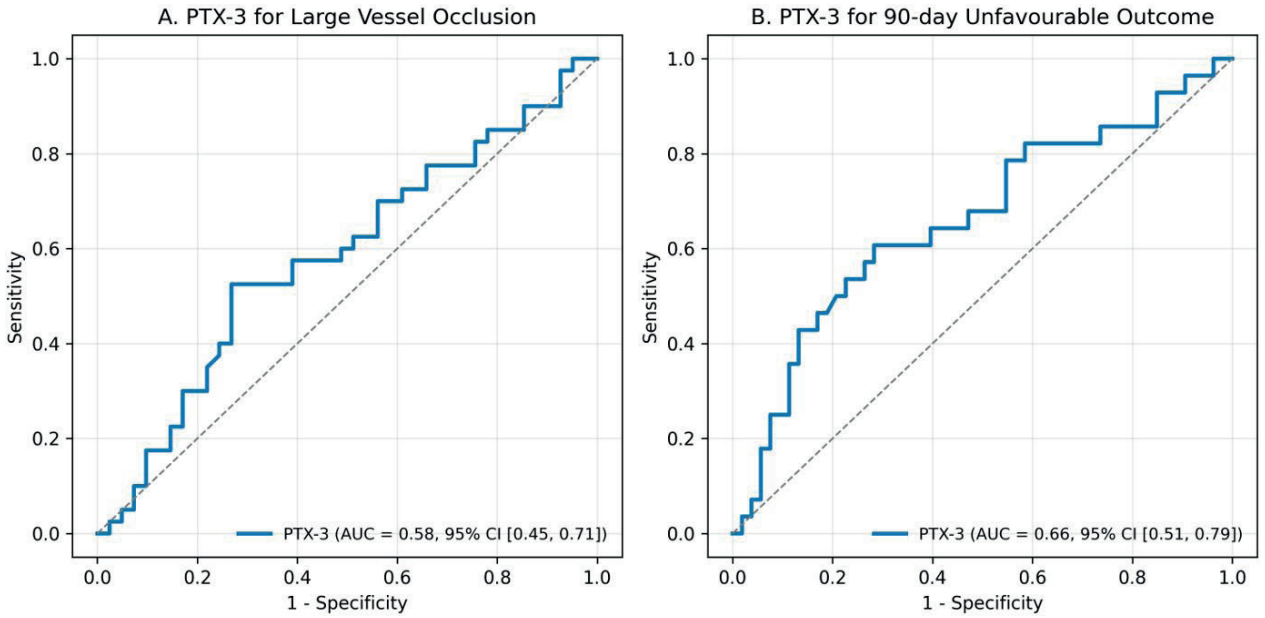

Figure 3. Receiver-operating-characteristic curves for serum pPentraxin-3.

Panel A: serum PTX-3 for discrimination of large-vessel occlusion (AUC = .58, 95% CI [.45, .71]). Panel B: serum PTX-3 for 90-day unfavourable outcome (AUC = .66, 95% CI [.51, .79]). Dashed 45° line = chance-level discrimination. Bootstrap percentile CIs (2,000 replicates).

The hierarchical multivariable sequence (Table 4, Models 1–4) demonstrates that the addition of admission NIHSS to the demographic block (Model 2) increased Nagelkerke's R^2 from .010 to .625 and produced an adjusted OR for NIHSS of 1.44 (95% CI [1.24, 1.67], p < .001); further addition of atrial fibrillation (Model 3) and then serum PTX-3 (Model 4) yielded only marginal gains in R^2 (to .643 and .647, respectively). In the fully adjusted model (Model 4), only NIHSS retained independent significance (adjusted OR = 1.42, 95% CI [1.21, 1.65], p < .001). Although atrial fibrillation was a strong univariate predictor of LVO (OR = 6.60), its effect attenuated substantially after adjustment for admission NIHSS (Model 3: OR = 2.73, p = .157), consistent with shared variance between stroke severity and cardioembolic etiology rather than independent predictive value. PTX-3 was non-significant in the fully adjusted model (OR = 0.998, 95% CI [0.993, 1.003], p = .486). Variance-inflation factors ranged from 1.86 to 8.06 (all < 10). The model showed good discrimination (C-statistic = .92; optimism-corrected .89) and acceptable calibration (Hosmer–Lemeshow p = .722). A likelihood-ratio test confirmed that adding PTX-3 did not improve model fit (LR $\chi^2(1) = 0.51$, p = .474).

Univariate and multivariable logistic regression for 90-day unfavorable outcome

Twenty-eight of the 81 patients with complete 90-day follow-up (34.6%) experienced an unfavorable outcome. Univariate and prespecified hierarchical multivariable logistic-regression estimates are reported in Table 5. In univariate analyses, serum PTX-3 was weakly but significantly associated with unfavorable outcome (OR = 1.004, 95% CI [1.000, 1.008], p = .041), as were admission NIHSS (OR = 1.33, 95% CI [1.18, 1.49], p < .001), baseline mRS (OR = 2.64, 95% CI [1.78, 3.93], p < .001), LVO status (OR = 19.00, 95% CI [5.00, 72.19], p < .001), and atrial fibrillation (OR = 4.15, 95% CI [1.60, 10.78], p = .003). Age and renal indices showed non-significant trend-level associations (age p = .094; urea p = .069; creatinine p = .083).

Table 4. Univariate and hierarchical multivariable logistic regression for large-vessel occlusion

Predictor	Univariate	p	Model 1 (Demographics)	Model 2 (+ NIHSS)	Model 3 (+ AF)	Model 4 (+ PTX-3)
	OR [95% CI]		OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Age (per year)	1.003 [0.969, 1.038]	.886	1.000 [0.965, 1.036]	0.975 [0.928, 1.025]	0.968 [0.916, 1.023]	0.969 [0.918, 1.024]
Sex (female = 1)	1.414 [0.585, 3.417]	.442	1.416 [0.575, 3.488]	2.958 [0.742, 11.793]	2.795 [0.674, 11.588]	2.850 [0.681, 11.922]
NIHSS (per point)	1.393 [1.217, 1.595]	< .001	—	1.436 [1.238, 1.666]***	1.398 [1.204, 1.624]***	1.415 [1.211, 1.653]***
AF (present = 1)	6.603 [2.466, 17.672]	< .001	—	—	2.733 [0.676, 11.052]	2.860 [0.699, 11.705]
PTX-3 (per 1 pg/mL)	1.002 [0.999, 1.005]	.248	—	—	—	0.998 [0.993, 1.003]
Baseline mRS (per point)	3.466 [2.151, 5.585]	< .001	—	—	—	—
Hemoglobin (per g/dL)	0.892 [0.689, 1.154]	.384	—	—	—	—
CRP (per mg/dL)	1.043 [0.795, 1.368]	.762	—	—	—	—
Creatinine (per mg/dL)	1.329 [0.448, 3.942]	.608	—	—	—	—
Troponin I (per ng/L)	0.991 [0.974, 1.009]	.340	—	—	—	—
Urea (per mg/dL)	1.009 [0.988, 1.031]	.402	—	—	—	—
Ferritin (per ng/mL) [c]	0.999 [0.995, 1.002]	.436	—	—	—	—
Model summary						
Nagelkerke R^2			.010	.625	.643	.647
Hosmer–Lemeshow p			.221	.819	.839	.722
C-statistic			.58	.92	.92	.92

N = 81 (40 LVO+, 41 LVO−). Variables were entered in four prespecified hierarchical blocks: Model 1 = age, sex (demographics); Model 2 = + NIHSS (clinical stroke severity); Model 3 = + AF (etiological indicator); Model 4 = + serum PTX-3 (primary biomarker). The univariate column reports the crude OR per one-unit increase for each candidate predictor. Optimism-corrected C-statistic for Model 4 (1,000 bootstrap replicates) = .89. Variance-inflation factors in Model 4: age 8.06, sex 1.86, NIHSS 3.88, AF 2.36, PTX-3 6.96 (all < 10). LR test, Model 3 vs. Model 4: $\chi^2(1) = 0.51$, p = .474. OR = odds ratio; CI = confidence interval; AF = atrial fibrillation (ECG or Holter); NIHSS = National Institutes of Health Stroke Scale; mRS = modified Rankin Scale; CRP = C-reactive protein. [c] n = 69 for ferritin (13 missing). *** p < .001.

Table 5. Univariate and hierarchical multivariable logistic regression for 90-day unfavourable outcome (mRS > 2)

Predictor	Univariate	p	Model 1 (Demographics)	Model 2 (+ NIHSS)	Model 3 (+ LVO)	Model 4 (+ PTX-3)
	OR [95% CI]		OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Age (per year)	1.035 [0.994, 1.077]	.094	1.036 [0.994, 1.079]	1.047 [0.984, 1.114]	1.049 [0.985, 1.118]	1.046 [0.981, 1.115]
Sex (female = 1)	1.348 [0.543, 3.345]	.521	1.648 [0.636, 4.274]	4.617 [0.849, 25.120]	4.037 [0.692, 23.530]	3.617 [0.627, 20.850]
NIHSS (per point)	1.326 [1.179, 1.491]	< .001	—	1.451 [1.223, 1.721]***	1.361 [1.134, 1.634]**	1.340 [1.118, 1.605]**
LVO status (LVO+ = 1)	19.00 [5.00, 72.19]	< .001	—	—	3.550 [0.639, 19.724]	4.005 [0.691, 23.202]
PTX-3 (per 1 pg/mL)	1.004 [1.000, 1.008]	.041	—	—	—	1.003 [0.997, 1.008]
AF (present = 1)	4.148 [1.596, 10.779]	.003	—	—	—	—
Baseline mRS (per point)	2.645 [1.781, 3.930]	< .001	—	—	—	—
Hemoglobin (per g/dL)	0.866 [0.653, 1.150]	.322	—	—	—	—
CRP (per mg/dL)	1.147 [0.901, 1.461]	.265	—	—	—	—
Creatinine (per mg/dL)	2.927 [0.869, 9.864]	.083	—	—	—	—
Urea (per mg/dL)	1.023 [0.998, 1.047]	.069	—	—	—	—
Troponin I (per ng/L)	0.996 [0.981, 1.011]	.580	—	—	—	—
Ferritin (per ng/mL) [c]	1.001 [0.998, 1.004]	.510	—	—	—	—
Model summary						
Nagelkerke R^2			.080	.652	.671	.681
Hosmer–Lemeshow p			.719	.119	.513	.185
C-statistic			.64	.93	.94	.95

N = 81 (28 unfavourable-outcome events / 53 favourable). Variables were entered in four prespecified hierarchical blocks: Model 1 = age, sex (demographics); Model 2 = + NIHSS (clinical stroke severity); Model 3 = + LVO status (vessel-occlusion indicator); Model 4 = + serum PTX-3 (primary biomarker). Optimism-corrected C-statistic for Model 4 (1,000 bootstrap replicates) = .87. Events-per-variable ratio = 28/5 = 5.6. LR test, Model 3 vs. Model 4: $\chi^2(1) = 1.13$, p = .289. OR = odds ratio; CI = confidence interval; AF = atrial fibrillation (ECG or Holter); NIHSS = National Institutes of Health Stroke Scale; LVO = large-vessel occlusion; mRS = modified Rankin Scale; CRP = C-reactive protein. [c] n = 69 for ferritin (13 missing). ** p < .01. *** p < .001.

The hierarchical multivariable sequence (Table 5, Models 1–4) showed that admission NIHSS was the dominant predictor: adding NIHSS to the demographic block (Model 2) raised Nagelkerke's R^2 from .080 to .652 (adjusted OR for NIHSS = 1.45, 95% CI [1.22, 1.72], p < .001). Adding LVO status (Model 3) increased R^2 to .671, and adding PTX-3 (Model 4) to .681. In the fully adjusted model (Model 4), NIHSS remained the only statistically significant independent predictor (adjusted OR = 1.34, 95% CI [1.12, 1.61], p = .002); the effect of LVO status attenuated (adjusted OR = 4.01, 95% CI [0.69, 23.20], p = .122); and the unadjusted PTX-3 association became non-significant (adjusted OR = 1.003, 95% CI [0.997, 1.008], p = .292). A likelihood-ratio test confirmed the absence of incremental value for PTX-3 (LR $\chi^2(1) = 1.13$, p = .289). The events-per-variable ratio (28/5 = 5.6) is below the conventional threshold of 10 and indicates that multivariable estimates should be interpreted cautiously.

DISCUSSION

In our study, we evaluated the ability of serum PTX-3 levels to confirm the diagnosis in patients with acute ischemic stroke with large vessel occlusion. The findings demonstrated that PTX-3 levels alone are not a sufficient biomarker to confirm the diagnosis of LVO. However, PTX-3 levels correlated with NIHSS at admission, suggesting that it may indirectly reflect stroke severity. When the relationship between PTX-3 and clinical outcome was examined, PTX-3 was not an independent prognostic marker.

PTX-3 is an acute phase reactant consisting of high molecular weight multimers connected to each other by interchain disulfide bonds, which is produced by the immune system as a response, particularly in atherosclerotic lesions, as well as in various cardiovascular and cerebrovascular diseases (11,12). In the pathophysiology of acute ischemic stroke, activation of the immune response against the resulting vascular inflammation leads to an increase in PTX-3 levels (13,14). High levels of CRP, one of the classical short pentraxins, have been associated with poor prognosis in ischemic stroke (15).

In the literature, PTX-3 has been reported to be associated with inflammation and atherosclerosis and to be a prognostic marker, especially in cardiovascular diseases (16,17). In a study conducted in patients with ischemic stroke, high PTX-3 levels were also significantly associated with the extent and severity of carotid artery stenosis (18). In a study examining patients with acute myocardial infarction, the prognostic value of PTX-3 was higher than that of troponin, creatine kinase, CRP, and N-terminal pro-brain natriuretic peptide (19). The findings regarding the relationship between PTX-3 levels and disease severity and clinical outcome in stroke patients are not consistent. While some studies have reported that PTX-3 levels are associated with increased disease severity and poor clinical outcome, other studies have stated that this relationship could not be demonstrated (8,10,20). Our study likewise found no significant relationship between clinical outcome and PTX-3.

In our study, the lack of a significant discriminative power of PTX-3 levels in predicting the presence of LVO may be because this biomarker mainly reflects the systemic inflammatory response. Large vessel occlusion, on the other hand, is primarily a local vascular event and involves complex pathophysiological processes that cannot be explained solely by the degree of inflammation. This situation may explain why PTX-3 is insufficient for discriminating the presence of LVO.

On the other hand, the positive correlation found between PTX-3 levels and NIHSS in our study suggests that this biomarker may be associated with disease severity. This finding is consistent with previous studies showing that PTX-3 is a marker reflecting vascular inflammatory burden and may indicate the degree of neurological damage. However, the finding that PTX-3 was not an independent marker of clinical outcome in multivariable analyses suggests that the prognostic value of this molecule is limited.

The relatively limited sample size of this study and the low number of events in multivariable analyses may limit the generalizability of the obtained results. In addition, the single-center design and the specific characteristics of the patient population may further limit the generalizability of the results to different populations.

CONCLUSION

Our study has demonstrated that PTX-3 levels are not a sufficient biomarker for the diagnosis of LVO in acute ischemic stroke. Although PTX-3 levels are associated with stroke severity, they are not an independent marker of clinical outcome. These findings suggest that PTX-3 has limited value in clinical decision-making and does not contribute to existing clinical parameters.

Ethical approval

This study has been approved by the Düzce University Non-Interventional Health Research Ethics Committee (approval date 27/07/2025, number 2025/165). Written informed consent was obtained from the participants.

Author contribution

Concept: AY; Design: AY, AÖ; Data Collection or Processing: HŞ; Analysis or Interpretation: AY; Writing: HT, AY, AÖ; Supervision: MA. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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