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A Discussion on ROC Curve: Exploring the Predictive Value of P-Selectin and PTX3 Levels in Patients with Nonvalvular Atrial Fibrillation Complicated with Ischemic Stroke

Qinhao Duanmu*

Department of Neurology, Emergency General Hospital, Ministry of Emergency Management, No. 29, Xiba Henan Li, Xiangheyuan Street, Chaoyang District, Beijing 1000028, China

***Corresponding author:** Qin Haoduanmu, 764334476@qq.com*

Abstract: *Objective*: To explore the predictive value of P-Selectin and Pentraxin 3 (PTX3) levels in patients with nonvalvular atrial fibrillation (NVAF) complicated with ischemic stroke using ROC curve analysis. *Methods*: Selected 48 patients with NVAF and ischemic stroke admitted to the hospital from June 2018 to December 2020 as the occurrence group, and 50 patients with NVAF without ischemic stroke during the same period as the nonoccurrence group. Clinical data of the two groups were collected. Serum CD62P and PTX3 levels were detected and compared between the two groups. Logistic regression analysis was used to analyze the risk factors for ischemic stroke in patients with NVAF, and the receiver operating characteristic curve (ROC) was used to evaluate the predictive value of serum CD62P and PTX3 levels for ischemic stroke in patients with NVAF. *Results:* The age, left atrial diameter (LAD), CHA2DS2VASc score, and serum CD62P and PTX3 levels of patients in the occurrence group were higher than those in the nonoccurrence group ($P < 0.05$). Logistic regression analysis showed that serum CD62P and PTX3 levels, CHA2DS2VASc score, LAD, and age were risk factors for ischemic stroke in patients with NVAF ($P < 0.05$). ROC analysis showed that the sensitivity, specificity, accuracy, and area under the curve (AUC) of serum CD62P and PTX3 in predicting ischemic stroke in NVAF patients were 80.72%/83.54%, 77.31%/74.29%, 79.35%/81.41%, and 0.769/0.787, respectively. The sensitivity, specificity, accuracy, and AUC of the combined prediction of the two were 90.36%, 68.75%, 87.91%, and 0.854, respectively. *Conclusion:* The abnormal increase in serum CD62P and PTX3 levels is related to NVAF patients complicated with ischemic stroke, and serum CD62P and PTX3 are risk factors for ischemic stroke in NVAF patients. The combination of the two has high clinical value in predicting ischemic stroke in NVAF patients.

Keywords: Nonvalvular atrial fibrillation; Ischemic stroke; P-Selectin; Pentraxin 3; Predictive value

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1. Introduction

Nonvalvular atrial fibrillation (NVAF) is a prevalent cardiac arrhythmia associated with a heightened risk of ischemic stroke [1]. Although clinical scoring systems such as CHA_2DS_2-VASc are widely used, their predictive accuracy remains suboptimal [2]. Emerging evidence suggests that biomarkers involved in thrombosis and inflammation, such as P-selectin (CD62P) and pentraxin 3 (PTX3), may enhance risk stratification [3,4]. This study investigates the predictive value of serum CD62P and PTX3 levels in NVAF patients with ischemic stroke using ROC curve analysis.

2. Materials and methods

2.1. General materials

From June 2018 to December 2020, 48 patients with NVAF and ischemic stroke admitted to the hospital were selected as the occurrence group, and 50 patients with NVAF without ischemic stroke during the same period were selected as the nonoccurrence group. The clinical data of the two groups were collected.

Inclusion criteria: (1) Based on the diagnostic criteria revised at the 6th National Cerebrovascular Disease Academic Conference, and confirmed by 24hour Holter monitoring, echocardiography, cranial MRI, and CT as NVAF or NVAF with ischemic stroke; (2) Patients in the occurrence group had their first episode of ischemic stroke, with the time from onset to hospitalization less than 24 hours; (3) Age between 18 and 80 years old; (4) Good compliance and signed informed consent.

Exclusion criteria: (1) Patients with intracranial hemorrhage or bleeding in the gastrointestinal or urinary system within the past 6 months; (2) Patients who had taken antibiotics or anticoagulant drugs within the past week; (3) Patients with rheumatic heart disease or artificial valve replacement; (4) Patients with severe liver and kidney dysfunction; (5) Patients with malignant tumors

2.2. Methods

2.2.1. Data collection

The clinical medical records of all patients were collected, including gender, age, body mass index (BMI), drinking history, smoking history, history of hypertension, diabetes, coronary heart disease, heart failure, duration of NVAF, left atrial diameter (LAD), left atrial diameter index (LADi), drug use (warfarin, aspirin, βblockers, calcium channel blockers), and CHA2DS2VASc score for thrombotic risk in atrial fibrillation. LAD was measured as the anteroposterior diameter of the left atrium. LADi was calculated as the mean left atrial diameter divided by body surface area. Body surface area (m^2) was calculated as 0.0061 × height (cm) + 0.0128 × weight (kg) − 0.1529.

2.2.2. Detection of serum CD62P and PTX3 levels

On the morning following admission, 4 mL of fasting venous blood was collected from all patients, placed in ethylenediaminetetraacetic acid anticoagulant tubes, and centrifuged at 3500 rpm for 10 minutes. The supernatant was collected and stored at 80 ℃ for later use. Enzyme-linked immunosorbent assay (ELISA) (reagent kits purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd.) was used to detect serum CD62P and PTX3 levels.

2.3. Statistical methods

SPSS 23.0 statistical software was used for data analysis. Measurement data were expressed as mean ± standard

deviation (SD) and analyzed using *t*-tests. Count data were expressed as cases (%). Logistic regression analysis was used to calculate the relative risk factors, odds ratios (OR), and 95% confidence intervals (CI) for ischemic stroke in patients with NVAF. The receiver operating characteristic curve (ROC) was used to evaluate the predictive ability of serum CD62P and PTX3 levels for ischemic stroke in patients with NVAF, and the area under the curve (AUC) was calculated. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of clinical data between the two groups

The age, LAD, CHA2DS2VASc score, and serum CD62P and PTX3 levels of patients in the occurrence group were higher than those in the nonoccurrence group ($P < 0.05$). There were no significant differences between the two groups in gender, BMI, drinking history, smoking history, history of hypertension, diabetes, coronary heart disease, heart failure, duration of NVAF, LADi, or the use of warfarin, aspirin, βblockers, and calcium channel blockers ($P > 0.05$). See **Table 1**.

Table 1. Comparison of clinical data between the two groups [mean ± SD, n (%)]

Item	Occurrence group (n = 48)	Non-occurrence group (n = 50)	t/χ^2 value	p value
Gender (Male)	32 (66.67)	29 (58.00)	0.783	0.376
Age (years old)	62.85 ± 6.34	59.14 ± 5.62	3.068	0.003
BMI (kg/m2)	23.04 ± 2.37	22.61 ± 1.89	0.995	0.322
Drinking History	33 (68.75)	26 (52.00)	2.868	0.09
Smoking History	31 (64.58)	24 (48.00)	2.735	0.098
Hypertension History	35 (72.92)	31 (62.00)	1.327	0.249
Diabetes History	16 (33.33)	12 (24.00)	1.045	0.307
Coronary Heart Disease History	25 (52.08)	19 (38.00)	1.963	0.161
Heart Failure History	15 (31.25)	8 (16.00)	3.171	0.075
Duration of NVAF (years)	1.05 ± 0.33	0.97 ± 0.21	1.438	0.154
LAD (mm)	41.53 ± 4.28	37.26 ± 3.09	5.68	< 0.001
LADi (mm/m^2)	26.15 ± 3.28	24.97 ± 2.89	1.892	0.062
Drug Use				
Warfarin	13 (27.08)	11 (22.00)	0.342	0.559
Aspirin	30 (62.50)	27 (54.00)	0.727	0.394
β-Blockers	29 (60.42)	28 (56.00)	0.196	0.658
Calcium Channel Blockers	19 (39.58)	16 (32.00)	0.613	0.434
CHA2DS2-VASc Score	3.12 ± 0.67	1.96 ± 0.41	10.385	< 0.001
CD62P (ng/mL)	18.93 ± 3.95	11.68 ± 2.74	10.593	< 0.001
PTX3 (ng/mL)	9.42 ± 1.46	5.89 ± 1.02	13.921	< 0.001

3.2. Logistic regression analysis of risk factors for ischemic stroke in patients with NVAF

Possible risk factors for ischemic stroke in patients with NVAF were used as independent variables (X), and whether ischemic stroke occurred as the dependent variable (Y). The related factors were assigned values, with ischemic stroke occurrence coded as 1 and nonoccurrence as 0. Logistic regression analysis was performed. Logistic regression analysis showed that serum CD62P and PTX3 levels, CHA2DS2VASc score, LAD, and age were risk factors for ischemic stroke in patients with NVAF ($P < 0.05$). See **Table 2** and **Table 3**.

Table 2. Variable assignment for logistic regression analysis

Variable	Variable Name	Assignment Method
Ischemic Stroke	Y	0 for non-occurrence, 1 for occurrence
PTX3	X1	Continuous Variable
CD62P	X2	Continuous Variable
CHA2DS2-VASc Score	X3	Continuous Variable
LAD	X4	Continuous Variable
Age	X5	Continuous Variable

Table 3. Logistic regression analysis of risk factors for ischemic stroke in patients with NVAF

Independent variable	β	SE	Wald	*P*-value	OR	95% CI
PTX3	1.223	0.276	19.635	< 0.001	3.397	1.541–5.416
CD62P	1.146	0.287	15.944	< 0.001	3.146	1.335–4.912
CHA2DS2-VASc Score	0.975	0.299	10.633	< 0.001	2.651	1.225–4.077
LAD	0.681	0.308	4.889	0.025	1.976	1.027–3.289
Age	0.594	0.317	3.511	0.037	1.811	1.004–2.868

3.3. ROC analysis of the predictive value of CD62P and PTX3 for ischemic stroke in patients with NVAF

The results of ROC analysis showed that the combination of CD62P and PTX3 had higher sensitivity and accuracy in predicting ischemic stroke in patients with NVAF than either marker alone. See **Table 4**.

Table 4. ROC analysis of the predictive value of CD62P and PTX3 levels for ischemic stroke in patients with NVAF

Indicator	Optimal cut-off point	Sensitivity	Specificity	Accuracy	AUC	95% CI
CD62P	16.21 ng/mL	80.72%	77.31%	79.35%	0.769	0.665–0.928
PTX3	8.05 ng/mL	83.54%	74.29%	81.41%	0.787	0.675–0.947
Combined	–	90.36%	68.75%	87.91%	0.854	0.716–0.963

4. Discussion

Nonvalvular atrial fibrillation (NVAF) represents a prevalent supraventricular tachyarrhythmia, marked by disorganized atrial electrical activation and loss of effective atrial mechanical contraction [1]. The incidence of

NVAF escalates with advancing age, exceeding 10% in individuals older than 70 years old [2]. This condition predisposes to thrombus formation, primarily through stasis in the left atrial appendage, culminating in embolic events such as ischemic stroke—a principal cause of morbidity and mortality in this patient cohort [2,5]. Consequently, identifying robust biomarkers for stratifying stroke risk is of paramount clinical importance.

P-selectin (CD62P), a cell adhesion molecule expressed on activated platelets and endothelial cells, is pivotal in mediating leukocyte-platelet aggregates and endothelial interactions [3,4,6]. Its release promotes a prothrombotic state by facilitating monocyte tissue factor expression and enhancing fibrin deposition [4,7]. Elevated soluble CD62P levels have been correlated with atrial thrombogenesis and ischemic stroke risk among NVAF patients, underscoring its potential utility as a predictive biomarker [7].

Pentraxin 3 (PTX3), an acute-phase inflammatory protein belonging to the long pentraxin family, is rapidly upregulated in response to vascular injury and inflammation [8,9]. PTX3 exhibits distinct structural and functional characteristics from the short pentraxin CRP, including localized production at inflammation sites and greater responsiveness to specific cardiovascular insults [10–12]. Elevated circulating PTX3 has been implicated in the pathogenesis of atherosclerosis, acute coronary syndromes, and ischemic stroke, reflecting its role in innate immunity and vascular inflammation [11–13].

Established clinical factors for stroke risk in NVAF include advanced age, female sex, and elevated CHA_2DS_2-VASc score [14,15]. Furthermore, left atrial dilation, quantified by LAD, serves as an indicator of atrial remodeling and stasis, and has been identified as an independent risk factor for thromboembolism [16].

The present study corroborates these findings, demonstrating significantly elevated serum CD62P and PTX3 levels in NVAF patients with ischemic stroke compared to those without. Furthermore, age, LAD, and CHA_2DS_2-VASc score were also significantly higher in the stroke group. Multivariable logistic regression analysis confirmed that each of these variables, including CD62P and PTX3, represents an independent risk factor for ischemic stroke [17,18].

ROC curve analysis demonstrated that both CD62P and PTX3 possess significant predictive capability for ischemic stroke, with AUC values of 0.769 and 0.787, respectively. Notably, the combination of these biomarkers yielded a superior AUC of 0.854, indicating enhanced discriminatory power over either marker alone. These observations suggest that CD62P and PTX3 contribute complementary pathophysiological information related to thrombotic and inflammatory pathways, respectively.

In conclusion, the integration of CD62P and PTX3 into existing risk stratification models may improve the identification of NVAF patients at high risk for ischemic stroke, thereby enabling more targeted and effective prophylactic therapy [19–21].

5. Conclusion

In summary, serum CD62P and PTX3 levels are elevated in NVAF patients with ischemic stroke, and both are risk factors for ischemic stroke in NVAF patients. Their combination has high predictive value for ischemic stroke in NVAF patients.

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