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Original Article

Post-stroke cognitive impairment in stroke survivors: correlations with serum fibrinogen, C-reactive protein, and interleukin-6

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Abstract: This study aimed to clarify the correlations of serum fibrinogen (FIB), C-reactive protein (CRP), and interleukin-6 (IL-6) with post-stroke cognitive impairment (PSCI) in stroke survivors. We selected 179 stroke patients visiting The Second People's Hospital of Huai'an (October 2023-October 2025) and allocated them as follows based on their Montreal Cognitive Assessment (MoCA) scores: PSCI group (n=90; MoCA <26 points) and non-PSCI group (n=89; MoCA ≥26 points). Serum FIB, CRP, and IL-6 at admission were detected. The correlations between these serum markers and MoCA scores were evaluated, and their predictive performance for PSCI occurrence and for mild-to-moderate PSCI was assessed using receiver operating characteristic (ROC) curves. Finally, we conducted univariate and multivariate analyses to explore factors influencing PSCI. The data showed markedly higher serum FIB, CRP, and IL-6 concentrations in PSCI patients compared to non-PSCI cases. All three markers exhibited a significant negative correlation with the MoCA score. The area under the curve (AUC) for PSCI predicted by FIB, CRP, and IL-6 ranged from 0.724 to 0.795, while their combined prediction (FIB+CRP+IL-6) reached an AUC of 0.895. For predicting mild-to-moderate severity, the AUCs of these markers used alone ranged from 0.706 to 0.761, and increased to 0.833 when combined. Age, National Institutes of Health Stroke Scale (NIHSS) score, FIB, CRP, and IL-6 were independent influencing factors of PSCI. Serum FIB, CRP, and IL-6 are strongly associated with PSCI occurrence and severity. They can serve as predictors of disease onset and mild-to-moderate severity, and are independent influencing factors for PSCI.

Keywords: Fibrinogen, C-reactive protein, interleukin 6, stroke, cognitive impairment, correlation

Introduction

Stroke is an acute cerebrovascular disease caused by a sudden blockage of cerebral blood flow or cerebral vascular rupture, leading to an ischemic or hemorrhagic stroke [1]. Ischemic stroke (IS) is the predominant type, diagnosed in 87% of all cases [2]. Stroke ranks as the second leading cause of death and the third leading cause of death and disability combined among non-communicable diseases worldwide. It also incurs high treatment costs, with global expenses projected to reach 900 billion US dollars [3]. Post-stroke cognitive impairment (PSCI), with an alarmingly high prevalence of 50% among stroke patients, is defined as cognitive impairment occurring after stroke in patients without a history of pre-stroke dementia [4]. Although PSCI may be reversible in the early stage, up to 33% of stroke survivors progress to dementia within 5 years [5]. This not only affects functional recovery and quality of life but also impedes overall outcome improvement [6]. There is an urgent need for non-invasive methods to identify novel predictors and modifiable risk factors for PSCI, which carries important clinical implications for reducing the stroke-associated disease burden [7].

Fibrinogen (FIB), a dimeric glycoprotein synthesized by the liver, is involved in the coagulation-fibrinolysis balance. In metabolic imbal-

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ance, it can promote post-stroke neuroinflammation through mechanisms such as blood-brain barrier (BBB) injury and fibrin deposition, thus elevating PSCI risk [8, 9]. FIB has been closely linked to PSCI in patients with ischemic cerebrovascular disease, with each 1 g/L increase potentially increasing PSCI risk by 1.92-fold; it may also negatively affect overall cognitive and visuospatial/executive functions [10]. As a marker of chronic systemic inflammation, C-reactive protein (CRP) can activate aberrant microglia through neuroinflammation, thus causing neuronal death and PSCI [11]. A study using UK Biobank data showed that high CRP levels are also an independent risk factor for young-onset dementia [12]. Interleukin (IL-6) is a key cytokine. When expressed at high levels in the brain, it can increase the likelihood of PSCI development by inducing neuronal damage, synaptic loss, and neuroinflammatory responses. This mechanism involves the activation of the Toll-like receptor 4 (TLR4)/myeloid differentiation factor 88/nuclear factor κB inflammatory pathway mediated by IL-6 [13]. A population-based cohort study strongly linked elevated plasma IL-6 levels to cognitive decline, brain atrophy, and an increased risk of all-cause dementia [14].

Given the limited evidence on the correlations of serum FIB, CRP, and IL-6 with PSCI in stroke survivors, this study aimed to conduct a correlation analysis to provide additional evidence and insights.

Materials and methods

Baseline information

The study population comprised 179 stroke patients treated at the Second People's Hospital of Huai'an, enrolled between October 2023 and October 2025. Patients were allocated to PSCI (n=90) and non-PSCI (n=89) groups based on their cognitive outcomes, evaluated at 6 months post-stroke using the Montreal Cognitive Assessment (MoCA) Scale. The PSCI patients included 59 males and 31 females, with a mean age of (61.3±17.39) years and a mean BMI of (23.66±2.46) kg/m^2. In the non-PSCI group, the average age, male-to-female ratio, and mean BMI were (57.53±6.30) years, 53:36, and (23.94±1.97) kg/m^2, respectively. This study was conducted with ethical approval from the Ethics Committee of the Second People's Hospital of Huai'an and strictly adhered to the Declaration of Helsinki.

Patient selection criteria

Inclusion criteria: confirmed diagnosis of stroke [15]; first-ever stroke; hospital admission within 72 hours of onset; age 18-80 years; clear consciousness and normal cognitive function upon admission; and complete clinical records.

Exclusion criteria: malignant tumors; serious heart, lung, or kidney dysfunction; inability to complete cognitive assessment due to severe disability or hemiplegia; history of craniocerebral injury or cerebral hemorrhage; dementia from other causes, autoimmune diseases, or intracranial infection; concurrent severe mental illness (e.g., depression, schizophrenia); cerebral hemorrhage, brain tumor, or other central nervous system (CNS) diseases; or acute/chronic infectious diseases.

Outcome measures

At 6 months post-stroke, patients' cognitive function was assessed using the MoCA scale [16]. The scale evaluates seven dimensions: language, naming, abstraction, attention, orientation, delayed recall, and visuospatial/execution. A score of 26 or above (maximum: 30 points) indicates normal cognitive function. Patients were assigned into non-PSCI (MoCA ≥26) and PSCI (MoCA <26) groups based on the assessment. In addition, patients were categorized into mild (18-25 points), moderate (10-17 points), or severe (<10 points) PSCI based on their MoCA scores. For patients with less than 12 years of education, 1 point was additionally added to the MoCA score to adjust for educational level.

After admission, patients underwent venipuncture for fasting cubital blood collection (4 mL). After centrifugation, the serum was separated for enzyme-linked immunosorbent assay (ELISA)-based FIB, CRP, and IL-6 quantification.

Statistical analysis

Data were analyzed using the SPSS 21.0 software package. Measurement data were tested for normality using the Shapiro-Wilk test. Categorical data were expressed as numbers

Table 1. Comparison of baseline characteristics between the two groups

Indicators	PSCI group (n=90)	Non-PSCI group (n=89)	χ^2/t	P
Age (years)	61.31±7.39	57.53±6.30	3.681	<0.001
Sex			0.689	0.407
Male	59 (65.56)	53 (59.55)		
Female	31 (34.44)	36 (40.45)		
Body mass index (kg/m^2)	23.66±2.46	23.94±1.97	0.840	0.402
Onset-to-admission time (h)	46.46±8.29	45.56±10.31	0.644	0.520
Educational level			4.367	0.037
Below senior high school	65 (72.22)	51 (57.30)		
Senior high school or above	25 (27.78)	38 (42.70)		
Diabetes	32 (35.56)	25 (28.09)	1.149	0.284
Hypertension	59 (65.56)	53 (59.55)	0.689	0.407
Smoking history	50 (55.56)	41 (46.07)	1.612	0.204
Alcoholism history	36 (40.00)	28 (31.46)	1.421	0.233
Cause of stroke			0.786	0.675
Large artery atherosclerosis	68 (75.56)	71 (79.78)		
Cardiogenic embolism	9 (10.00)	9 (10.11)		
Small vessel occlusion	13 (14.44)	9 (10.11)		
Lesion location			0.941	0.625
Anterior circulation	57 (63.33)	61 (68.54)		
Posterior circulation	28 (31.11)	22 (24.72)		
Anterior and posterior circulation	5 (5.56)	6 (6.74)		
NIHSS (points)	12.57±3.42	10.46±3.36	4.163	<0.001

Notes: PSCI, post-stroke cognitive impairment; NIHSS, National Institutes of Health Stroke Scale.

and percentage (n/%). Normally distributed continuous data were presented as mean ± standard deviation (SD), and non-normally distributed data as median (interquartile range) [M(Q1, Q3)]. Between-group comparisons for categorical data were performed using the chi-square test. For continuous data, between-group comparisons were conducted using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. In this study, only the MoCA scores were non-normally distributed. Correlations between serum FIB, CRP, and IL-6 and MoCA scores were assessed using Spearman's correlation analysis. Their predictive value for PSCI occurrence and mild-to-moderate PSCI was evaluated using receiver operating characteristic (ROC) curves, and performance was measured by areas under the curve (AUCs). The AUC for combined variables was obtained from ROC analysis based on predictive probabilities derived from logistic regression. Influencing factors for PSCI were identified using univariate and multivariate logistic regression analyses. A *P*-value <0.05 was considered statistically significant.

Results

Baseline information

The PSCI (n=90) and non-PSCI (n=89) groups were defined based on patients' MoCA scores at 6 months post-stroke. The two groups did not differ significantly in sex, BMI, onset-to-admission time, diabetes, hypertension, smoking history, alcohol consumption history, stroke cause, or lesion location (P>0.05). However, PSCI patients were older and had higher NIHSS scores (P<0.001), and a higher proportion of patients had education below high school (P=0.037; **Table 1**).

Serum FIB, CRP, and IL-6 levels

PSCI patients exhibited notably higher serum FIB, CRP, and IL-6 levels than their non-PSCI counterparts (P<0.001; **Figure 1**).

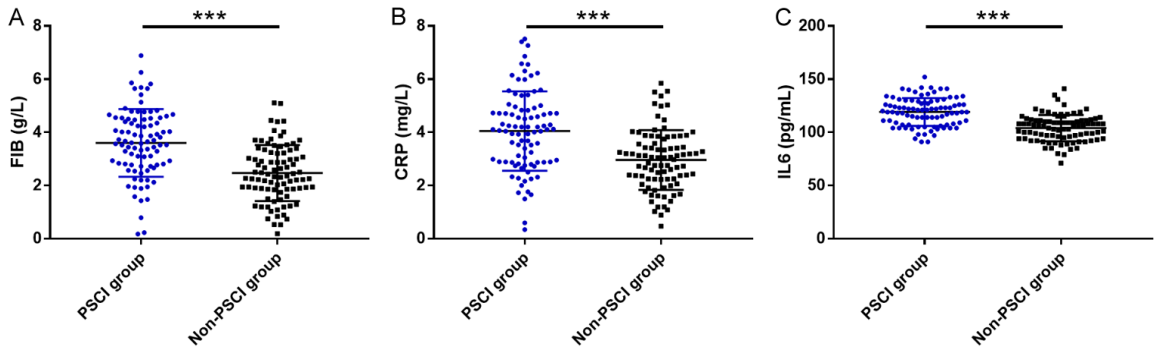


Figure 1. Comparison of serum FIB (A), CRP (B), and IL-6 (C) levels between PSCI and non-PSCI groups. Notes: FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment; ***P<0.001.

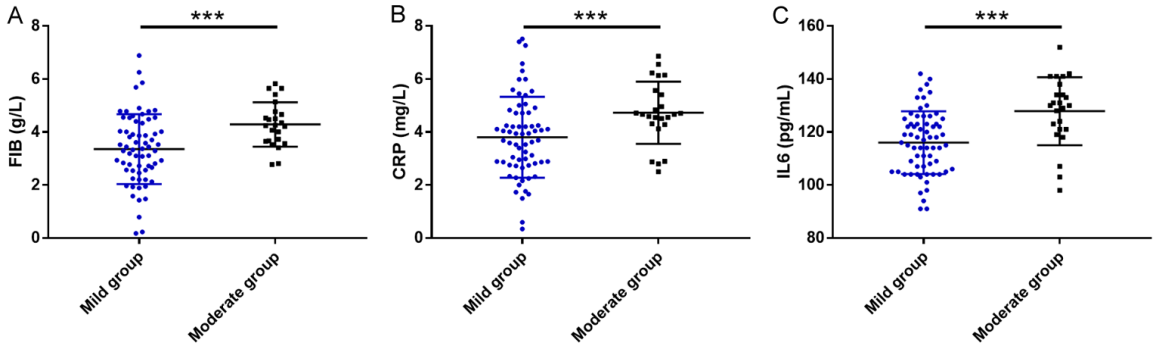


Figure 2. Comparison of serum FIB (A), CRP (B), and IL-6 (C) levels between mild and moderate groups. Notes: FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment; ***P<0.001.

Table 2. Correlation of serum FIB, CRP, and IL-6 with MoCA scores

Indicators	r	P
FIB (g/L) vs. MoCA (points)	-0.383	<0.001
CRP (mg/L) vs. MoCA (points)	-0.363	<0.001
IL-6 (pg/mL) vs. MoCA (points)	-0.429	<0.001

Notes: FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; MoCA, Montreal Cognitive Assessment.

Serum FIB, CRP, and IL-6 in groups with varying PSCI severity

Based on MoCA scores, patients were further divided into mild (n=66) and moderate (n=24) PSCI groups. The moderate group showed higher serum FIB, CRP, and IL-6 than the mild group, with the differences reaching statistical significance (P<0.001; **Figure 2**).

Correlation of serum FIB, CRP, and IL-6 with MoCA

According to Spearman's correlation, serum FIB, CRP, and IL-6 were significantly and negatively correlated with MoCA scores in stroke patients (r=-0.383, P<0.001; r=-0.363, P< 0.001; r=-0.429, P<0.001; **Table 2**).

Efficacy of serum FIB, CRP, and IL-6 in predicting PSCI

For predicting PSCI occurrence, the AUC of FIB was 0.762 (95% CI: 0.692-0.832), with a sensitivity of 73.03% and specificity of 68.89% at an optimal cutoff of 3.08 g/L. For CRP, the AUC was 0.724 (95% CI: 0.649-0.799), with 84.27% sensitivity and 58.89% specificity at an optimal cutoff of 3.91 mg/L. The AUC of IL-6 was 0.795 (95% CI: 0.730-0.860), with 80.90% sensitivity and 68.89% specificity at an optimal cutoff value of 113.50 pg/mL. Combined use yielded the best performance (AUC=0.895, 95% CI: 0.848-0.942), with 92.13% sensitivity and 76.67% specificity at a cutoff of 0.38 (**Figure 3**; **Table 3**).

Efficacy of serum FIB, CRP, and IL-6 in predicting mild-to-moderate PSCI

We further divided the stroke cohort (n=179) into mild (n=66) and moderate (n=24) PSCI

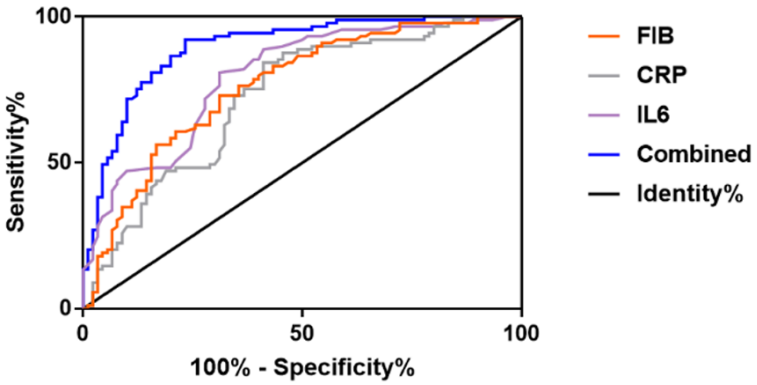


Figure 3. ROC curves of serum FIB, CRP, IL-6, and their combination in predicting PSCI. Notes: ROC, receiver operating characteristic; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment.

Table 3. Predictive performance of serum FIB, CRP, and IL-6 for PSCI

Indicators	AUC	95% CI	Optimal cutoff	Sensitivity	Specificity
FIB (g/L)	0.762	0.692-0.832	3.08	73.03%	68.89%
CRP (mg/L)	0.724	0.649-0.799	3.91	84.27%	58.89%
IL-6 (pg/mL)	0.795	0.730-0.860	113.50	80.90%	68.89%
Combined	0.895	0.848-0.942	0.38	92.13%	76.67%

Notes: AUC, area under the curve; CI, confidence interval; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment.

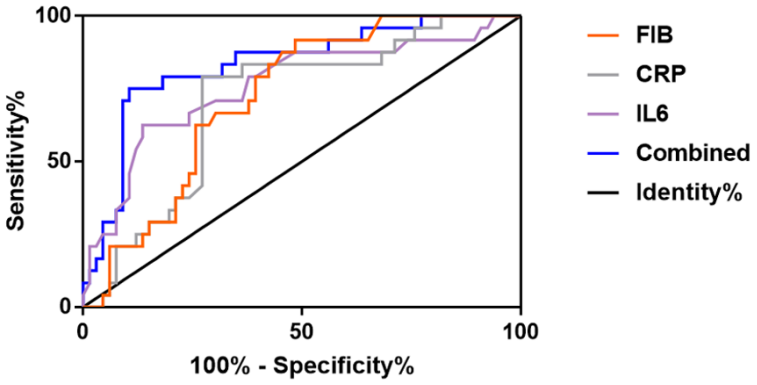


Figure 4. ROC curves of serum FIB, CRP, IL-6, and their combination in predicting mild-to-moderate PSCI. Notes: ROC, receiver operating characteristic; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment.

groups; no severe PSCI cases were included. Severe PSCI cases were not enrolled for two reasons: (1) Severe PSCI is typically associated with severe aphasia, attention deficits, or impaired consciousness, making it difficult for patients to complete all MoCA subtests; (2) This study focused on mild-to-moderate PSCI, a population with potential for cognitive rehabilitation and clinical intervention, to evaluate the predictive efficacy of serum inflammatory markers in this stage. The performance of the three markers in predicting PSCI severity was evaluated using ROC curves. For FIB, the AUC was 0.723 (95% CI: 0.618-0.828), with a sensitivity of 91.67% and specificity of 51.52% at an optimal cutoff of 3.39 g/L; the AUC of CRP was 0.706 (95% CI: 0.590-0.822), with 79.17% sensitivity and 72.73% specificity at an optimal cutoff of 4.27 mg/L; the AUC of IL-6 was 0.761 (95% CI: 0.641-0.881), with a sensitivity of 62.50% and specificity of 86.36% at an optimal cutoff of 127.50 pg/mL. The combined use of the three markers achieved the best performance for predicting mild-to-moderate PSCI (AUC=0.833, 95% CI: 0.736-0.931), with 75.00% sensitivity and 89.39% specificity at a cutoff of 0.37 (**Figure 4**; **Table 4**).

Univariate and multivariate analyses mining influencing factors of PSCI

Univariate logistic regression identified age (OR=1.084, 95% CI: 1.035-1.134, P=0.001), educational level (OR=0.516, 95% CI: 0.277-0.963, P=0.038), admission NIHSS score (OR=1.201, 95% CI: 1.094-1.318, P<0.001), FIB (OR=2.304, 95% CI: 1.698-3.126, P<0.001), CRP (OR=1.887, 95% CI: 1.452-2.452, P<0.001), and IL-6 (OR=1.097, 95% CI: 1.064-1.130, P<0.001) as factors influencing PSCI. After adjustment for confounders in multivariate logistic regression, age (OR=1.138, 95% CI: 1.059-1.224, P<0.001), NIHSS score (OR=1.263, 95% CI: 1.089-1.464,

Table 4. Predictive performance of serum FIB, CRP, and IL-6 for mild-to-moderate PSCI

Indicators	AUC	95% CI	Optimal cutoff	Sensitivity	Specificity
FIB (g/L)	0.723	0.618-0.828	3.39	91.67%	51.52%
CRP (mg/L)	0.706	0.590-0.822	4.27	79.17%	72.73%
IL-6 (pg/mL)	0.761	0.641-0.881	127.50	62.50%	86.36%
Joint detection	0.833	0.736-0.931	0.37	75.00%	89.39%

Notes: AUC, area under the curve; CI, confidence interval; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6; PSCI, post-stroke cognitive impairment.

Table 5. Univariate analysis of factors associated with PSCI

Indicators	B	SE	WALD	P	OR	95% CI
Age (years)	0.080	0.023	11.928	0.001	1.084	1.035-1.134
Educational level	-0.661	0.318	4.316	0.038	0.516	0.277-0.963
NIHSS (points)	0.183	0.048	14.749	<0.001	1.201	1.094-1.318
FIB (g/L)	0.834	0.156	28.699	<0.001	2.304	1.698-3.126
CRP (mg/L)	0.635	0.134	22.605	<0.001	1.887	1.452-2.452
IL-6 (pg/mL)	0.092	0.015	35.841	<0.001	1.097	1.064-1.130

Notes: PSCI, post-stroke cognitive impairment; OR, odds ratio; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6.

Table 6. Multivariate analysis of independent risk factors for PSCI

Indicators	B	SE	WALD	P	OR	95% CI
Age (years)	0.130	0.037	12.249	<0.001	1.138	1.059-1.224
Educational level	-0.582	0.506	1.322	0.250	0.559	0.207-1.507
NIHSS (points)	0.233	0.076	9.535	0.002	1.263	1.089-1.464
FIB (g/L)	0.852	0.217	15.396	<0.001	2.344	1.532-3.587
CRP (mg/L)	0.712	0.191	13.944	<0.001	2.038	1.402-2.961
IL-6 (pg/mL)	0.100	0.020	24.852	<0.001	1.106	1.063-1.150

Notes: PSCI, post-stroke cognitive impairment; OR, odds ratio; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale; FIB, fibrinogen; CRP, C-reactive protein; IL-6, interleukin-6.

P=0.002), FIB (OR=2.344, 95% CI: 1.532-3.587, P<0.001), CRP (OR=2.038, 95% CI: 1.402-2.961, P<0.001), and IL-6 (OR=1.106, 95% CI: 1.063-1.150, P<0.001) remained statistically significant, whereas educational level (P=0.250) lost significance (**Tables 5**, **6**).

Discussion

Many previous studies have focused on identifying potential biomarkers of cognitive impairment. Take the study by Angley et al. [17] for example, which indicated no significant correlation of serum zinc concentration and dietary zinc intake with cognitive impairment. Chang et al. [18], however, reported that increased serum BDNF levels were significantly correlated with a reduced risk of PSCI within three months, suggesting that BDNF may be a potential predictor of PSCI in IS patients with hypertension. Another cross-sectional study found that elevated serum iron levels were strongly associated with a lower risk of early-onset PSCI, indicating that low serum iron levels may help identify early-stage PSCI [19]. This study correlates serum FIB, CRP, and IL-6 with PSCI in stroke survivors and conducts validation.

First, PSCI was associated with older age, higher NIHSS scores, and lower educational level. Mechanistically, older age is associated not only with degenerative brain structural changes, such as reduced hippocampal and gray matter volume, but also with comorbidities like diabetes, which together aggravate brain injury and promote PSCI onset [20, 21]. A higher admission NIHSS score generally reflects greater brain injury severity, which can aggravate cognitive impairment [22]. Lower educational level may indicate reduced cognitive reserve, making it harder for the brain to compensate or recruit alternative neural circuits, thereby increasing PSCI risk [23].

Furthermore, stroke patients who developed PSCI had significantly higher serum FIB, CRP, and IL-6 levels, and these levels were even higher in those with more severe PSCI, suggesting that these markers may mediate PSCI onset and progression. FIB can leak through the damaged BBB and deposit in the CNS, thus inducing neuroinflammation and neurodegeneration and increasing the likelihood of PSCI [24]. CRP and IL-6 can transmit inflammatory signals to the CNS via three routes: active

transport across the BBB, vagal afferent pathways, and volume diffusion to extra-BBB organs. Consequently, microglia and astrocytes are activated to induce a neuroinflammatory microenvironment that adversely affects synaptic plasticity and cognitive function, ultimately promoting the process of PSCI [25]. Supporting our findings, FIB is reported to be elevated in PSCI patients compared to their non-PSCI counterparts, which can be used to predict PSCI after acute IS while acting as an independent influencing factor of PSCI [26]. A bidirectional Mendelian randomization study investigated the causality between CRP and PSCI and confirmed that CRP was significantly associated with prospective memory, genetic proxy cognitive performance, and fluid intelligence, suggesting a possible bidirectional causal relationship [27]. In the report of Wu et al. [28], CRP and IL-6 were indicated to be expressed at markedly higher levels in PSCI patients than in healthy controls, which is highly consistent with the phenomena observed in this study.

Additionally, we found a significant negative correlation between each of the three serum markers and MoCA scores, suggesting that higher levels of these markers are closely associated with worse cognitive function. Liu et al. [29] identified high plasma FIB as an independent risk factor for PSCI in acute IS patients, and found it negatively correlated with cognitive function, which supports our findings. Yang et al. [30] reported an inverse association between CRP and certain cognitive abilities in apolipoprotein E ε4 allele (APOE ε4) homozygotes, consistent with our findings. Zhao et al. [14] also reported that IL-6 was negatively correlated with performance in pair matching, numeric/prospective memory, and reaction time tests, corroborating our findings. IL-6 can stimulate hepatic synthesis of FIB and CRP. FIB can then penetrate the brain parenchyma, activate microglia, and up-regulate IL-6 following stroke-induced BBB disruption; it can also promote neuronal overexpression of IL-6 through NF-κB signaling [9, 31]. Within the brain, IL-6 further disrupts the BBB, promoting FIB exudation. This establishes a self-reinforcing cycle that further amplifies neuroinflammation, leading to neuronal damage, synapse loss, and ultimately PSCI [32, 33].

ROC analysis showed that the AUCs of FIB, CRP, and IL-6 alone for predicting PSCI ranged from 0.724 to 0.795, whereas their combined AUC reached 0.895, with both high sensitivity (92.13%) and specificity (76.67%). For mild-to-moderate PSCI prediction, the AUCs of FIB, CRP, and IL-6 alone ranged from 0.706 to 0.761, and their combined use increased the AUC to 0.833. Among them, FIB had the highest sensitivity (91.67%) but the lowest specificity (51.52%) in predicting mild-to-moderate PSCI; the sensitivity (79.17%) and specificity (72.73%) of CRP in predicting mild-to-moderate PSCI were both at a moderate level; IL-6 had a relatively high specificity (86.36%) but the lowest sensitivity (62.50%); the joint prediction yielded the best specificity (89.39%) and acceptable sensitivity (75.00%), indicating a better balance between sensitivity and specificity. Zhuang et al. [34] reported an AUC of 0.764 for FIB in predicting cognitive impairment in patients with diabetic peripheral neuropathy, similar to our AUC of 0.762 for PSCI. Zhu et al. [35] found that the combined AUC of S100B, GFAP, and IL-6 for PSCI prediction was 0.887, higher than their individual AUCs (0.792, 0.752, and 0.732). This is consistent with our combined AUC of 0.895 for FIB, CRP, and IL-6.

Several studies have explored the clinical utility of FIB, CRP, IL-6, and other biomarkers. For example, Wolszczak-Biedrzycka et al. [36] noted the utility of CRP, IL-6, and CRP/IL-6 in predicting symptom severity and mortality risk in COVID-19 patients. Ma et al. [37] reported that the combination of procalcitonin (PCT), CRP, and FIB was feasible for early pneumonia screening, achieving the highest diagnostic efficiency (AUC=0.964) in differentiating viral from bacterial infection in severe pneumonia. Jia et al. [38] also reported that the serum C1q-to-CRP ratio (CCR) can diagnose periprosthetic joint infection in revision arthroplasty, with a sensitivity of 95.77% and a negative predictive value of 96.20% at a cutoff of 0.03.

Univariate and multivariate analyses showed that age, NIHSS score, FIB, CRP, and IL-6 were independent risk factors for PSCI. Based on these findings, early cognitive rehabilitation (e.g., digital intervention based on virtual reality, computer-assisted cognitive therapy, and robot-assisted therapy) and aerobic exercise (gait training, cycling, aquatic therapy) are rec-

ommended to reduce PSCI risk, especially for high-risk patients with advanced age, high NIHSS scores, and elevated inflammatory markers (FIB, CRP, and IL-6) [39, 40]. Yang et al. [41] also identified age, CRP, diabetes, and hypertension are strong predictors of PSCI, complementing our results.

The innovative aspects of this study include: First, serum FIB, CRP, and IL-6 are innovatively combined to predict PSCI, reaching exceptional performance (AUC=0.895). This finding has strong potential for clinical transformation, as it supports the integration of multiple serological inflammatory markers in clinical practice to improve screening efficiency. Second, we innovatively analyzed the performance of these markers in screening mild-to-moderate PSCI, providing a quantitative basis for the early identification of intermediate-risk PSCI. Third, we identified independent risk factors for PSCI, offering indirect evidence for PSCI prevention through targeted anti-inflammatory interventions.

Several limitations of this work should be acknowledged. First, the sample may not be fully representative because no severe PSCI cases were included. Future studies should include patients across all PSCI severity levels to improve representativeness and to evaluate the predictive efficacy of these markers for severe PSCI prediction. Second, this is a single-center exploratory analysis with limited sample size. We did not perform internal cross-validation or Bootstrap bias correction for the joint prediction model, which may carry a risk of overfitting. As this is a preliminary exploration, the stability and generalization of the joint model require further validation in large-sample, multi-center studies. Finally, we did not conduct stratified analysis by onset-to-admission time. Although this variable did not differ significantly between groups and was not included the multivariate model, its potential confounding or modifying effects in specific subgroups cannot be entirely excluded owing to the limited sample size. In the future, a larger sample size is needed for further analysis and verification.

In conclusion, serum FIB, CRP, and IL-6 are elevated in patients with PSCI, especially in those with moderate PSCI, and are negatively correlated with cognitive function. The combination of these three markers may serve as an auxiliary predictor of PSCI occurrence and severity (mild to moderate). Moreover, older age, higher NIHSS scores, and elevated FIB, CRP, and IL-6 are independent risk factors for PSCI.

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Disclosure of conflict of interest

None.

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