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ORIGINAL ARTICLE

Predictive Value of Combined Vitamin D, hs-CRP, and Cerebral Hemodynamic Parameters for Mid- to Long-Term Recurrence Risk of Ischemic Stroke

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ABSTRACT

Background: **This study aimed to investigate the value of combined detection of vitamin D, high-sensitivity C-reactive protein (hs-CRP), and cerebral hemodynamic parameters in predicting the mid- to long-term recurrence risk of ischemic stroke.**

Methods: **A total of 409 patients with a first acute ischemic stroke were enrolled. Serum 25-hydroxyvitamin D [25(OH)D], hs-CRP levels, and transcranial Doppler examination were performed within 72 hours of symptom onset; the maximum pulsatility index (PImax) on the affected side was recorded. Recurrence events were recorded during a 12-month follow-up. Cox proportional hazards models were used to analyze the association of the three indicators with recurrence. A combined prediction model was constructed, and its discriminative ability (area under the curve [AUC], concordance index [C-index]), calibration (Brier score, calibration-in-the-large), and clinical net benefit (decision curve analysis) were evaluated.**

Results: **Within 12 months, 66 patients (16.1%) experienced recurrence. Multivariable Cox analysis, adjusted for confounders such as age and National Institutes of Health Stroke Scale score, showed that 1 standard deviation (SD) increase in PImax (hazard ratio [HR] = 2.53, 95% confidence interval [CI]: 1.92 - 3.34, p < 0.001), 1 SD increase in ln(hs-CRP) (HR = 2.38, 95% CI: 1.75 - 3.24, p < 0.001), and 1 SD decrease in 25(OH)D (HR = 2.21, 95% CI: 1.68 - 2.91, p < 0.001) were all independent risk factors for recurrence. The AUC for the three-indicator combined model was 0.869, while the AUC for the five-indicator model (including age and National Institutes of Health Stroke Scale score) was 0.875, with a C-index of 0.848. Both models demonstrated good calibration and showed significant net benefit within the 10% - 30% recurrence risk threshold range. Kaplan-Meier analysis revealed that the groups with high PImax, high hs-CRP, and low 25(OH)D levels had significantly higher 12-month cumulative recurrence rates (all Log-rank p < 0.001).**

Conclusions: **This study confirms that vitamin D deficiency, systemic inflammation activation, and elevated cerebrovascular resistance are independently associated with mid- to long-term ischemic stroke recurrence. The combined prediction model based on 25(OH)D, hs-CRP, and PImax demonstrates high differentiation ability for predicting recurrence risk. Integrating metabolic, inflammatory, and hemodynamic information can effectively identify high-risk populations for stroke recurrence, providing a basis for individualized risk stratification and precise secondary prevention.**

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Supplementary Data

Table S1. Fine-Gray competing-risk sensitivity analysis for 12-month recurrence.

Variable	SHR	95% CI	p-value
Age (per 1-SD increase)	1.30	1.02 - 1.64	0.032
NIHSS (per 1-SD increase)	1.40	1.11 - 1.76	0.005
ln(hs-CRP) (per 1-SD increase)	2.37	1.78 - 3.16	< 0.001
25(OH)D (per 1-SD decrease)	2.20	1.67 - 2.90	< 0.001
PImax (per 1-SD increase)	2.53	1.94 - 3.30	< 0.001

Death without prior recurrence was treated as the competing event.
SHR: Subdistribution hazard ratio, CI: Confidence interval, NIHSS: National institutes of health stroke scale, PImax: Pulsatility index with affected-side preference.