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Development and Validation of a Predictive Scale for Stroke and Cognitive Impairment in Atherothrombotic Carotid Disease

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ABSTRACT

Atherothrombotic lesions of the internal carotid arteries are among the leading causes of ischemic stroke and cognitive decline. Traditional assessment focused primarily on the degree of stenosis fails to reflect the complex interplay between vascular, metabolic, and neurocognitive factors that determine clinical outcomes. This study was aimed at developing and validating a predictive scale that integrates structural, functional, biochemical, and cognitive parameters to improve individual risk assessment and optimize preventive strategies.

A prospective cohort of 357 patients with atherothrombotic extracranial arterial disease was examined. Independent predictors of ischemic stroke and cognitive decline were identified using multivariate Cox regression analysis adjusted for age, sex, hypertension, diabetes, and smoking. The evaluated factors included bilateral or combined internal carotid and vertebral artery stenosis, cerebrovascular reserve (CVR), plaque morphology, high-sensitivity C-reactive protein (hs-CRP), and Montreal Cognitive Assessment (MoCA) score. The discriminative performance of the models was analyzed using receiver operating characteristic (ROC) curves, and a Predictive Risk Scale (PRS) was derived based on Cox regression coefficients and validated during 12 months of clinical follow-up.

The analysis revealed that combined internal carotid and vertebral artery stenosis (HR 1.93, $p<0.001$), decreased CVR below 30% (HR 1.65, $p=0.003$), and unstable plaques (HR 1.48, $p=0.006$) were the strongest predictors of ischemic stroke. For cognitive impairment, MoCA score below 24 (HR 1.67, $p=0.004$) and age above 70 years (HR 1.34, $p=0.039$) were significant independent factors. The integrated PRS demonstrated an area under the ROC curve of 0.88 (95% CI 0.84–0.92), with sensitivity of 84% and specificity of 81%. The use of the PRS with individualized prevention reduced the incidence of cerebrovascular events from 23.3% to 6.7% within 12 months of observation. Economic efficiency analysis indicated that implementation of the scale decreased direct treatment costs by approximately 65% per patient, largely through reduced rates of stroke-related disability and hospitalization.

The developed Predictive Risk Scale incorporates anatomical (stenosis and plaque morphology), functional (cerebrovascular reserve), biochemical (hs-CRP), and cognitive (MoCA) variables, providing a comprehensive approach to evaluating stroke and cognitive decline risk. Integration of this scale into clinical practice enables physicians to identify high-risk individuals, personalize preventive measures, and rationally allocate medical resources. The findings demonstrate that a multifactorial model significantly surpasses traditional stenosis-based assessment, facilitating more accurate prognosis, reduced stroke incidence, preserved cognitive health, and improved cost-effectiveness. The proposed scale may serve as a valuable tool for both primary and secondary prevention of cerebrovascular and cognitive complications in patients with atherothrombotic carotid disease.

KEYWORDS

Ischemic stroke, carotid atherosclerosis, atherothrombosis, cerebrovascular reserve, cognitive impairment, MoCA, predictive risk scale, Cox regression, ROC analysis, plaque instability, vertebral artery stenosis, individualized prevention, cost-effectiveness, vascular-cognitive interaction, risk stratification.

INTRODUCTION

Atherothrombotic lesions of the internal carotid arteries represent one of the most important causes of ischemic stroke and progressive cognitive decline, posing a major public health challenge worldwide. Despite the widespread use of imaging-based assessments of carotid stenosis, these measurements alone do not adequately reflect the multifactorial mechanisms that determine cerebrovascular outcomes. Stroke risk is not solely a function of arterial narrowing but results from a combination of hemodynamic insufficiency, plaque instability, inflammation, and impaired neurovascular coupling. Similarly, cognitive impairment in patients with carotid disease is closely related to chronic cerebral hypoperfusion and microembolization, which are not captured by anatomical parameters alone. In this context, the development of an integrated predictive system capable of evaluating multiple dimensions of cerebrovascular pathology has become an urgent clinical and scientific task [1].

The relationship between atherothrombotic carotid disease, ischemic stroke, and cognitive decline has evolved from a purely anatomical understanding of stenosis to a multifactorial concept that includes hemodynamic, inflammatory, and neurocognitive mechanisms. Abboud et al. (2020) demonstrated that both symptomatic and asymptomatic carotid atherosclerosis significantly increase stroke risk, emphasizing the prognostic value of plaque instability and inflammation. Bonati, Nederkoorn, and Kappelle (2018) similarly argued that management of asymptomatic stenosis requires individualized assessment beyond lumen narrowing, while de Weerd et al. (2010) confirmed that asymptomatic carotid lesions are common in older adults, highlighting the need for early risk

identification [2].

Functional parameters such as cerebrovascular reserve (CVR) have been shown to improve prediction accuracy. Markus and Cullinane (2001) found that impaired CVR independently predicts stroke and TIA, a finding supported by Xu et al. (2022), who linked reduced CVR to cognitive decline in carotid stenosis. Morphological features are equally important: Marnane et al. (2016) demonstrated that plaque inflammation and instability predict early stroke recurrence, and Saba et al. (2019) confirmed the clinical utility of advanced plaque imaging .

The connection between vascular pathology and cognition was explored by Gorelick et al. (2011) and Chollet and Tatu (2019), who concluded that chronic hypoperfusion and microembolization contribute to progressive cognitive decline even in the absence of overt infarction. Yong, Lee, and Lee (2017) also found that cognitive dysfunction often precedes ischemic events in carotid atherosclerosis.

Inflammation plays a key mechanistic role: Spence (2020) and Rosenberg (2017) described how systemic and neurovascular inflammation accelerate plaque progression and impair the blood–brain barrier, contributing to both ischemic and cognitive outcomes. Bath and Wardlaw (2015) noted that interventions targeting vascular inflammation and endothelial dysfunction could prevent such complications .

Standardization of structural assessment remains essential. Touboul et al. (2012) provided international consensus criteria for carotid intima-media thickness measurement, ensuring comparability across studies and supporting early detection of subclinical disease .

The present study aimed to create and validate a predictive scale that integrates anatomical, hemodynamic, biochemical, and cognitive markers to improve the accuracy of risk stratification for ischemic stroke and cognitive decline among patients with atherothrombotic extracranial artery disease. A prospective cohort of 357 patients was enrolled and followed for a 12-month period. All patients underwent duplex ultrasonography of the internal carotid and vertebral arteries, quantitative assessment of cerebrovascular reserve (CVR) using transcranial Doppler and vasodilatory testing, biochemical analysis of high-sensitivity C-reactive protein (hs-CRP), and neuropsychological evaluation using the Montreal Cognitive Assessment (MoCA) [5]. The presence and morphology of atherosclerotic plaques were assessed using high-resolution ultrasound criteria to distinguish stable and unstable formations.

Statistical analysis was performed using multivariate Cox regression modeling to identify independent predictors of ischemic stroke and cognitive impairment, adjusting for age, sex, arterial hypertension, diabetes mellitus, and smoking status. Receiver operating characteristic (ROC) curve analysis was then employed to evaluate the discriminatory power of individual and combined predictors. Regression coefficients (β values) derived from the Cox model were used to construct a Predictive Risk Scale (PRS) that assigned weighted scores to each factor, allowing clinicians to calculate a cumulative risk index for every patient [6].

The multivariate analysis demonstrated that combined internal carotid and vertebral artery stenosis was the most significant predictor of ischemic stroke, increasing risk by nearly twofold (HR 1.93, $p<0.001$). Decreased cerebrovascular reserve below 30% (HR 1.65, $p=0.003$) and the presence of unstable atherosclerotic plaques (HR 1.48, $p=0.006$) were also strongly associated with future stroke events. For cognitive decline, the most significant independent variables were a baseline MoCA score below 24 (HR 1.67, $p=0.004$) and age over 70 years (HR 1.34, $p=0.039$) [7]. Elevated hs-CRP levels above 3 mg/L were linked to a moderate but clinically relevant increase in both stroke and cognitive risk, reflecting the inflammatory component of atherothrombosis.

ROC analysis confirmed that the predictive accuracy of single anatomical parameters, such as the degree of stenosis, was limited (AUC 0.67). When functional parameters like CVR were added, model performance improved substantially (AUC 0.78). The combination of plaque morphology and CVR increased predictive power to AUC 0.81, while inclusion of both carotid and vertebral artery data resulted in AUC 0.86. The highest prognostic accuracy was achieved by incorporating MoCA results into the composite model, yielding an AUC of 0.88 (95% CI 0.84–0.92) with sensitivity of 84% and specificity of 81%. These findings highlight the strong interaction between vascular and cognitive factors in determining outcomes for patients with extracranial atherosclerosis.

The PRS was subsequently applied in a 12-month clinical validation phase. Two groups of patients were compared: one managed according to the PRS with individualized preventive measures (n=30) and another receiving standard care without stratification (n=30). In the PRS group, the incidence of ischemic stroke was 3.3% and transient ischemic attack (TIA) 6.7%, compared to 13.3% and 10% respectively in the standard-care group. Thus, the overall rate of cerebrovascular events decreased more than threefold, from 23.3% to 6.7%, demonstrating the strong preventive efficacy of the PRS-guided approach.

An economic analysis further supported the clinical benefits of the new model. The cost of treating one patient under standard management averaged 2,894,000 Uzbek soums, whereas the cost for a patient managed with PRS-based diagnostics and prevention was 1,009,000 soums, including the cost of extended diagnostics. The calculated economic efficiency was 65%, indicating a nearly two-third reduction in direct healthcare expenditures per patient. The reduction in stroke incidence and disability also translated into substantial social benefits by preserving employment and reducing the long-term burden on healthcare and social welfare systems.

The Predictive Risk Scale assigns numerical values to major determinants of vascular and cognitive deterioration, including unilateral, bilateral, and combined stenosis patterns, cerebrovascular reserve, plaque instability, inflammatory activity, and baseline cognitive status. The total score allows rapid risk classification into low, moderate, and high categories. Patients with high scores require intensive preventive measures such as optimization of blood pressure, lipid profile, and glycemic control, strict lifestyle modification, and evaluation for potential surgical intervention through carotid endarterectomy or stenting. Regular reassessment of PRS every 6–12 months provides dynamic monitoring of cerebrovascular and cognitive risk trajectories.

The results of this study confirm that the progression and complications of atherothrombotic carotid disease are determined not by a single anatomic factor but by the integration of multiple interacting mechanisms. The proposed predictive scale enables early identification of high-risk individuals, allowing preventive strategies to be tailored before irreversible neurological damage occurs. By combining vascular imaging, physiological testing, inflammation markers, and neurocognitive assessment, this approach bridges the gap between traditional vascular diagnostics and modern concepts of brain health preservation.

In conclusion, the Predictive Risk Scale developed and validated in this study offers a practical, evidence-based tool for clinicians to evaluate the combined risk of ischemic stroke and cognitive impairment in patients with atherothrombotic carotid disease. Incorporating this multifactorial model into everyday clinical practice significantly enhances preventive efficiency, reduces the frequency of cerebrovascular events, preserves cognitive performance, and optimizes resource utilization. The integration of structural, functional, biochemical, and cognitive domains into a single predictive framework represents a step forward in personalized cerebrovascular medicine and sets a foundation for

the future of precision prevention in vascular neurology.

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