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Predictive Risk Scale for Stroke and Cognitive Impairment: Development, Validation, and Clinical Application

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Abstract: Stroke and related cognitive impairments remain among the leading causes of disability and mortality worldwide. The development of reliable tools for early risk prediction represents a key priority in modern neurology and preventive medicine. This study presents the development and validation of a predictive risk scale based on a comprehensive assessment of clinical, laboratory, and neuropsychological parameters, including blood pressure levels, lipid profile, inflammatory markers, comorbidities, and indicators of short- and long-term memory. A total of 420 patients with various vascular risk factors were enrolled. Multifactorial analysis using ROC curves was conducted to determine optimal threshold values for identifying groups with low, moderate, and high risk of stroke and cognitive decline. The results demonstrated high sensitivity (89%) and specificity (84%) of the proposed scale. The clinical use of the developed predictive scale enhances the accuracy of individualized prognosis and contributes to the optimization of secondary prevention strategies for stroke and vascular dementia.

Keywords: Stroke, cognitive impairment, risk scale, prediction, validation, vascular dementia, neuropsychology, prevention.

Introduction: Stroke continues to be one of the most urgent medical and social problems of the 21st century, ranking second among the causes of death and first among the causes of adult disability worldwide. The World Health Organization estimates that every year about 15 million people suffer a stroke, of which 5 million die and another 5 million remain permanently disabled. In parallel, the prevalence of post-stroke cognitive impairment has grown to alarming proportions, with nearly one-third of survivors developing vascular cognitive dysfunction or dementia within five years after the initial event. This dual burden—motor and cognitive—creates enormous pressure on healthcare systems and families alike. Hence, the modern concept of cerebrovascular disease prevention is not limited to traditional control of risk factors but requires an integrated approach that includes early identification of individuals predisposed to both stroke and cognitive decline.

Literature review

The literature converges on a multifactorial, brain–vascular paradigm of stroke and vascular cognitive impairment. Large global syntheses quantify population risk and regional heterogeneity, with INTERSTROKE and the Global Burden of Disease analyses underscoring hypertension, diabetes, dyslipidemia, and inflammation as dominant, modifiable drivers of incident stroke and post-event disability. Consensus statements and commission reports extend this view to cognition, arguing that vascular mechanisms—small-vessel disease, hypoperfusion, and endothelial dysfunction—substantially contribute to cognitive decline and are viable prevention targets. Cohort and biomarker studies from Framingham and related work highlight

inflammatory and metabolic markers alongside lipids as independent predictors of both stroke and dementia trajectories, while neuropathology reviews detail white-matter lesions, microinfarcts, and mixed Alzheimer–vascular patterns that map onto executive and memory deficits. Clinical studies in Russian-language sources complement this by emphasizing recurrent-stroke predictors and early neuropsychological screening, and recent updates on secondary prevention stress tighter blood-pressure and lipid targets, antithrombotic stewardship, and lifestyle interventions. Emerging methods using machine learning show promise for individualized prediction but face issues of generalizability and clinical integration. Together, these strands justify integrated risk tools that combine hemodynamic, metabolic, inflammatory, and cognitive measures, and they identify gaps in external validation across diverse populations and in the routine incorporation of cognitive endpoints into vascular risk stratification [1,2,3,4,5,6,7,8,9,10].

Background and Rationale

The pathogenesis of stroke and vascular cognitive impairment (VCI) involves a complex interplay of hemodynamic, metabolic, inflammatory, and neurodegenerative mechanisms. Chronic hypertension and atherosclerosis lead to endothelial dysfunction, impaired cerebral autoregulation, and microangiopathy, which gradually reduce the brain's reserve capacity. Simultaneously, dyslipidemia, insulin resistance, and systemic inflammation accelerate atherothrombosis and increase the likelihood of both ischemic and hemorrhagic events. Neuroinflammation, oxidative stress, and neuronal apoptosis contribute to progressive cognitive decline, particularly in domains of attention, memory, and executive function.

Traditional risk scoring systems such as Framingham Stroke Risk Profile and CHA_2DS_2-VASc are widely used for cardiovascular events but fail to capture the neurocognitive dimension of cerebrovascular disease. Furthermore, most existing tools were developed on Western populations and may not adequately reflect regional differences in lifestyle, genetics, and comorbidities. The present study therefore aimed to create a regionally validated predictive risk scale that integrates vascular and neuropsychological determinants, offering a holistic view of cerebrovascular risk.

Materials and Methods

The study was conducted from 2021 to 2024 at the Neurology and Preventive Medicine Departments of the Samarkand State Medical University and collaborating clinical centers. It included 420 participants aged 45–80 years with at least one vascular risk factor. The mean age was 62.3±9.7 years; 48.6% were male and 51.4% female. Exclusion criteria were a previous history of stroke, transient ischemic attack, major psychiatric illness, or neurodegenerative disease such as Alzheimer's or Parkinson's.

Each participant underwent detailed anamnesis, clinical examination, and laboratory testing. The variables measured included blood pressure (office and ambulatory), lipid profile (total cholesterol, HDL, LDL, triglycerides), fasting glucose, glycated hemoglobin (HbA1c), C-reactive protein (CRP), and interleukin-6 (IL-6). Carotid Doppler ultrasonography was performed to assess intima-media thickness and the presence of atherosclerotic plaques. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Trail Making Test (TMT).

All data were analyzed using SPSS 27.0. Continuous variables were expressed as means ± standard deviation. Logistic regression was used to determine independent predictors of stroke and cognitive impairment. ROC curve analysis was applied to assess predictive accuracy. A prognostic risk scale was constructed by assigning weighted scores to each independent variable based on its odds ratio (OR) in the regression model. The resulting cumulative score was used to classify participants into low, moderate, and high-risk groups.

Results

The multivariate logistic regression analysis identified six independent predictors that were significantly associated with the combined endpoint of stroke occurrence and measurable cognitive decline over the three-year follow-up period. Each of these predictors was included in the final prognostic model after rigorous statistical testing for collinearity, confounding, and internal consistency.

Age over 60 years (OR 2.4; 95% CI 1.7–3.6; $p < 0.01$) was found to be a strong determinant of both cerebrovascular and cognitive outcomes. Individuals older than sixty were more than twice as likely to develop either an ischemic or hemorrhagic stroke as compared to younger individuals. This remained significant after adjustment for other factors such as hypertension and diabetes. The age factor reflects the cumulative effect of endothelial injury, oxidative stress, and structural degeneration of cerebral vessels, leading to reduced perfusion and brain plasticity. In parallel, the process of neurodegeneration—synaptic loss, white matter rarefaction, and mitochondrial dysfunction—predisposes elderly individuals to cognitive deterioration even before the occurrence of

clinically apparent vascular events [11].

Systolic blood pressure above 140 mmHg (OR 3.1; 95% CI 2.1–4.5; p < 0.001) emerged as the most influential modifiable variable. Persistent hypertension leads to microvascular remodeling, lipohyalinosis, and increased cerebral arterial stiffness, all of which compromise autoregulatory capacity. The patients with poor blood pressure control demonstrated not only an elevated risk of stroke but also impaired executive function and slower cognitive processing. The results confirm that both chronic pressure overload and short-term variability contribute to the pathogenesis of small vessel disease and cognitive decline [12].

Total cholesterol exceeding 5.5 mmol/L (OR 1.9; 95% CI 1.2–3.0; p = 0.02) was identified as another significant predictor. Hypercholesterolemia accelerates atherosclerosis and endothelial dysfunction, promoting plaque formation in carotid and intracranial arteries. This contributes to subclinical brain infarctions and hypoperfusion, which gradually result in deterioration of memory and attention. In this cohort, individuals with high LDL and low HDL cholesterol levels displayed greater carotid intima-media thickness and unstable plaques, confirming the link between lipid metabolism and neurovascular damage [13].

C-reactive protein levels higher than 3 mg/L (OR 2.6; 95% CI 1.6–3.9; p = 0.001) indicated that inflammation plays a pivotal role in the mechanism connecting vascular pathology and cognitive disorders. Participants with increased CRP showed Doppler signs of endothelial dysfunction and MRI evidence of periventricular white matter lesions. The inflammatory process is believed to accelerate endothelial damage, increase permeability of the blood-brain barrier, and stimulate deposition of amyloid proteins within cerebral small vessels. These interlinked mechanisms enhance susceptibility to both vascular dementia and ischemic injury.

Diabetes mellitus (OR 3.8; 95% CI 2.4–5.2; p < 0.001) produced the strongest independent metabolic influence on the risk model. Chronic hyperglycemia causes nonenzymatic glycation of proteins, thickening of capillary basement membranes, and microangiopathy. The resulting diffuse ischemia and reduced neuronal energy metabolism contribute to cognitive impairment independent of major strokes. Patients with poor glycemic control (HbA1c > 7.5%) performed significantly worse on memory and attention tests, demonstrating the direct cognitive consequences of metabolic dysregulation [14].

A Montreal Cognitive Assessment (MoCA) score below 26 (OR 2.9; 95% CI 1.8–4.3; p < 0.01) also showed predictive significance. Individuals with subthreshold baseline cognitive performance were almost three times more likely to experience subsequent cognitive deterioration or cerebrovascular events. This finding suggests that mild cognitive impairment may serve as an early marker of cerebrovascular insufficiency or small vessel disease. The inclusion of this neuropsychological parameter in the scale expands the predictive framework beyond traditional cardiovascular indicators.

Each of the six predictors was assigned a weight from one to three points according to its odds ratio and relative contribution to risk estimation. Diabetes mellitus and uncontrolled hypertension were allocated three points each, elevated CRP two points, age over sixty two points, hypercholesterolemia two points, and a low MoCA score three points. The cumulative total ranged from zero to fifteen points, allowing classification of patients into three easily distinguishable categories.

Low risk (0–5 points) corresponded to a predicted probability of less than ten percent. Most participants in this group remained clinically stable during follow-up, with minimal changes in cognitive scores. Moderate risk (6–10 points) represented a ten to thirty percent probability, and these individuals frequently exhibited subclinical vascular changes such as carotid plaque formation or mild cognitive slowing. High risk (11–15 points) indicated a probability exceeding thirty percent. This category contained the majority of participants who suffered strokes or a significant reduction in MoCA and MMSE scores over three years.

Receiver operating characteristic curve analysis confirmed the high discriminative capacity of the model, with an area under the curve of 0.91 (95% CI: 0.87–0.94). The model's sensitivity reached 89 percent, meaning that nearly nine out of ten high-risk individuals were correctly identified, while specificity of 84 percent indicated a low false-positive rate. The positive predictive value was 82 percent, and the negative predictive value was 90 percent, confirming that low-risk patients were reliably identified. Calibration analysis using the Hosmer–Lemeshow test showed good agreement between predicted and observed event rates ($\chi^2 = 6.4$; p = 0.42). The internal consistency of the scale, measured by Cronbach's alpha coefficient, was 0.87, indicating strong internal reliability.

For external validation, the model was tested in an independent cohort of two hundred patients observed for three years. Fifty-eight individuals (29 percent) developed either stroke or significant cognitive decline defined as a decrease of at least three points in MoCA score. The prognostic scale correctly classified eighty-six percent of these cases as moderate or high risk at

baseline, confirming reproducibility. Kaplan–Meier survival analysis demonstrated a clear gradient between risk categories: three-year event-free survival was 94 percent in the low-risk group, 77 percent in the moderate-risk group, and 52 percent in the high-risk group (log-rank $p < 0.001$).

The findings revealed that participants with higher total scores not only had an increased frequency of stroke but also exhibited progressive deterioration in executive, memory, and visuospatial functions, reflecting the characteristic pattern of vascular cognitive impairment. The gradual transition from subclinical vascular dysfunction to manifest cognitive decline highlights the overlapping mechanisms of macrovascular and microvascular brain injury.

Taken together, the results of this multivariate analysis and validation confirm that the proposed predictive scale possesses strong prognostic power, stability, and practical value. The integration of demographic, metabolic, inflammatory, and neuropsychological indicators allows for a holistic estimation of cerebrovascular risk and provides clinicians with a simple yet precise instrument for early prevention and individualized intervention.

Table 1. Predictive Factors of Stroke and Cognitive Decline: Multivariate Analysis Results

Predictor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value	Interpretation Summary
Age > 60 years	2.4	1.7–3.6	< 0.01	Older individuals have more than twice the risk of stroke and cognitive decline due to endothelial injury and neurodegeneration.
Systolic BP > 140 mmHg	3.1	2.1–4.5	< 0.001	Hypertension is the most influential modifiable factor, linked to small vessel disease and cognitive impairment.
Total cholesterol > 5.5 mmol/L	1.9	1.2–3.0	0.02	Hypercholesterolemia promotes atherosclerosis and subclinical brain infarctions leading to memory decline.
C-reactive protein > 3 mg/L	2.6	1.6–3.9	0.001	Inflammatory processes accelerate endothelial damage and increase susceptibility to vascular dementia.
Diabetes mellitus	3.8	2.4–5.2	< 0.001	Chronic hyperglycemia leads to microangiopathy and worsened cognitive function independent of stroke.
MoCA score < 26	2.9	1.8–4.3	< 0.01	Baseline cognitive impairment predicts further cognitive deterioration and cerebrovascular events.

Discussion

The predictive risk scale developed in this study provides a novel multidimensional approach to vascular and cognitive risk assessment. Unlike conventional models that primarily rely on cardiovascular parameters, this tool integrates markers of neuropsychological performance and inflammation—two domains that are increasingly recognized as central to cerebrovascular pathology.

The inclusion of cognitive testing, particularly MoCA scores, reflects the growing understanding that subtle cognitive deficits may precede overt cerebrovascular events. Chronic inflammation, as indicated by elevated CRP and IL-6, emerged as a strong and independent predictor, confirming the role of systemic inflammatory processes in the pathogenesis of both atherosclerosis and neurodegeneration. These findings are consistent with recent studies demonstrating that elevated CRP levels correlate with white matter lesions, reduced hippocampal volume, and slower cognitive processing speed [15].

In practical terms, the proposed scale has significant clinical utility. In primary care, it enables physicians to quickly identify high-risk patients who require aggressive management of modifiable factors—strict blood pressure control, lipid-lowering therapy,

glycemic optimization, and anti-inflammatory interventions. In neurology clinics, it can be used for long-term monitoring of patients with mild cognitive impairment or subclinical vascular changes. The scale is also suitable for use in community screening programs and telemedicine platforms, where it can guide referral decisions.

Implementation and Preventive Strategies

For individuals classified as high risk, personalized prevention programs should be initiated. These may include:

- Intensive antihypertensive therapy targeting systolic BP < 130 mmHg.
- Statin treatment to reduce LDL cholesterol below 1.8 mmol/L.
- Antiplatelet therapy in the presence of carotid atherosclerosis.
- Structured cognitive training to enhance executive and memory functions.
- Nutritional modification emphasizing the Mediterranean diet.
- Regular aerobic exercise (150 minutes per week).
- Smoking cessation and moderation of alcohol intake.

Integrating these interventions with periodic reassessment using the predictive scale allows continuous monitoring of progress and adjustment of treatment strategies.

Limitations and Future Directions

The study's main limitation is its regional focus, which may limit the generalizability of results to other ethnic groups and healthcare environments. The relatively short follow-up period (three years) restricts long-term outcome evaluation. Additionally, neuroimaging data such as MRI markers of cerebral small vessel disease were not included in the final model, though their incorporation could further improve predictive accuracy. Future studies should expand to multicenter, multinational cohorts and test the scale's performance across different healthcare settings.

Another promising direction involves integrating genetic and epigenetic data, such as APOE polymorphisms and methylation markers, into predictive models. Artificial intelligence and machine learning algorithms could also enhance the precision of risk prediction by automatically analyzing large datasets and identifying complex nonlinear interactions between variables.

Conclusion

The developed predictive risk scale for stroke and cognitive impairment represents a practical, validated, and highly accurate instrument for early risk assessment. Its use allows physicians to move beyond the traditional cardiovascular model and adopt a comprehensive approach that integrates vascular, metabolic, inflammatory, and neuropsychological factors. Implementing this tool in clinical practice may significantly improve primary and secondary prevention, reduce the incidence of stroke, and mitigate the growing global burden of vascular cognitive disorders.

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