Integrated Vascular–Cognitive Assessment: Toward a Predictive Model for Stroke and Cognitive Decline in Atherothrombotic Carotid Disease

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Abstract: Recent evidence demonstrates that the risk of ischemic stroke and cognitive decline in patients with atherothrombotic carotid disease cannot be explained by stenosis severity alone. Modern studies emphasize the multifactorial nature of cerebrovascular risk, encompassing hemodynamic insufficiency, plaque instability, systemic inflammation, and impaired neurocognitive reserve. This review synthesizes current literature on the anatomical, functional, biochemical, and cognitive determinants of cerebrovascular outcomes. Research by Abboud et al. (2020) and Bonati et al. (2018) highlights the prognostic value of plaque morphology and individualized management of carotid stenosis. Functional studies by Markus and Cullinane (2001) and Xu et al. (2022) demonstrate that reduced cerebrovascular reserve predicts both ischemic events and cognitive decline. Inflammatory mechanisms identified by Spence (2020) and Rosenberg (2017) further explain disease progression and neuronal injury. The integration of these findings supports the creation of comprehensive predictive models combining carotid imaging, cerebrovascular reactivity, systemic biomarkers, and cognitive assessment. Such models provide superior prognostic accuracy, enable earlier risk stratification, and promote personalized prevention strategies aimed at reducing stroke incidence and preserving cognitive health.

Keywords:
atherothrombotic carotid disease, ischemic stroke, cognitive impairment, cerebrovascular reserve, plaque instability, inflammation, predictive model, risk stratification, MoCA, vascular cognition

Atherothrombotic carotid disease represents one of the leading causes of ischemic stroke and cognitive deterioration worldwide, contributing significantly to disability and mortality among the aging population. Traditionally, the risk of cerebrovascular

events has been evaluated predominantly based on the degree of luminal stenosis in the internal carotid arteries. While this anatomical parameter remains important, it provides only a partial understanding of the complex mechanisms leading to ischemia and brain dysfunction. Over the past two decades, numerous clinical and experimental studies have demonstrated that stroke and cognitive decline are multifactorial phenomena, arising from a combination of hemodynamic compromise, inflammatory processes, plaque instability, and neurovascular uncoupling. This shift from a purely morphological to an integrated pathophysiological model has transformed both diagnostic and prognostic approaches to carotid atherosclerosis.

Evidence from large-scale analyses confirms the strong link between carotid atherosclerosis and ischemic stroke risk. Abboud et al. (2020) performed a systematic review and meta-analysis that synthesized data from multiple prospective cohorts and established that both symptomatic and asymptomatic carotid atherosclerosis markedly increase the likelihood of ischemic events. Their results demonstrated that plaque composition and systemic inflammatory activity are often stronger predictors of stroke than stenosis degree alone. This insight supports a move toward comprehensive risk models that integrate biological and structural variables. Bonati, Nederkoorn, and Kappelle (2018) reached a similar conclusion in their clinical review, emphasizing that the management of asymptomatic stenosis must be based on individualized assessment that includes plaque vulnerability, cerebrovascular reactivity, and patient-specific comorbidities rather than rigid surgical criteria.

The functional integrity of the cerebral circulation has emerged as a central determinant of outcome in patients with carotid disease. Markus and Cullinane (2001) were among the first to show that severely impaired cerebrovascular reserve predicts both stroke and transient ischemic attack independently of stenosis severity. This finding introduced the concept that vascular reactivity, reflecting the brain’s ability to maintain perfusion under stress, is a critical prognostic marker. More recent research by Xu et al. (2022) extended these results, revealing that reduced cerebrovascular reactivity not only increases stroke risk but also correlates strongly with progressive cognitive decline in patients with carotid stenosis. These data confirm that chronic hypoperfusion contributes to neuronal damage and that hemodynamic assessment should be incorporated into predictive scales for both vascular and cognitive outcomes.

Inflammatory and immune mechanisms play an equally important role in the progression of carotid atherothrombosis. Spence (2020) described resistant

atherosclerosis as a condition driven by persistent inflammation, infection, and immune activation. His work highlighted that systemic inflammatory markers, such as high-sensitivity C-reactive protein (hs-CRP), serve as independent predictors of plaque progression and vascular complications. Similarly, Rosenberg (2017) demonstrated that neuroinflammation and disruption of the blood–brain barrier mediate secondary neuronal injury, thereby linking systemic vascular pathology with cognitive dysfunction. These findings have expanded the understanding of atherothrombosis from a purely mechanical obstruction to a chronic inflammatory process that affects both the vasculature and the brain.

The morphology and stability of carotid plaques are critical components of stroke risk prediction. Marnane et al. (2016) demonstrated that plaques with a thin fibrous cap, large lipid core, and inflammatory infiltration are associated with early stroke recurrence in patients with symptomatic carotid stenosis. This study confirmed that morphological instability, rather than absolute stenosis severity, determines embolic potential. Building upon these observations, Saba et al. (2019) reviewed the rapid advances in carotid wall imaging technologies, including high-resolution magnetic resonance and contrast-enhanced ultrasound. They concluded that multiparametric imaging integrating plaque composition, neovascularization, and perfusion metrics significantly enhances diagnostic and prognostic accuracy. These methods enable clinicians to identify high-risk patients who may benefit from early intervention even when stenosis is moderate.

The cognitive consequences of carotid atherothrombosis have gained increasing attention as evidence accumulates linking vascular pathology to neurocognitive decline. Gorelick et al. (2011), in their landmark American Heart Association statement, introduced the concept of vascular cognitive impairment and dementia, emphasizing that vascular pathology contributes substantially to the global burden of cognitive decline. Chollet and Tatu (2019) elaborated on these mechanisms, showing that chronic hypoperfusion, microembolization, and endothelial dysfunction collectively lead to progressive impairment in attention, memory, and executive function. Yong, Lee, and Lee (2017) provided additional clinical evidence demonstrating that cognitive deficits are frequently observed even in patients without overt ischemic events, suggesting that cognitive screening should be integrated into the routine evaluation of individuals with carotid atherosclerosis.

Population-level data further illustrate the widespread and often silent burden of carotid disease. De Weerd et al. (2010), through a meta-analysis of population studies, reported that asymptomatic carotid stenosis affects up to three percent of adults over sixty years of age, with prevalence increasing sharply in those with cardiovascular comorbidities. Such findings underscore the importance of developing predictive tools capable of identifying high-risk individuals before the onset of stroke or cognitive impairment. Standardized measurements of vascular structure, such as those proposed by Touboul et al. (2012) in the Mannheim consensus on intima-media thickness, have improved the comparability of studies and enabled earlier detection of subclinical atherosclerosis.

The convergence of these research directions suggests that stroke and cognitive decline share common vascular mechanisms. Chronic cerebral hypoperfusion, oxidative stress, endothelial dysfunction, and systemic inflammation collectively damage both large and small cerebral vessels, leading to neuronal loss and impaired cognitive processing. Pharmacological strategies aimed at restoring endothelial function, improving perfusion, and reducing inflammation, as reviewed by Bath and Wardlaw (2015), provide additional support for the integrated management of vascular and cognitive health.

This accumulation of evidence points to the need for a predictive model that reflects the multifactorial nature of carotid disease. Such a model should combine anatomical information about stenosis and plaque morphology with functional data on cerebrovascular reserve, biochemical markers of inflammation, and neurocognitive performance measures such as the Montreal Cognitive Assessment (MoCA). Integrating these components into a unified predictive scale would allow clinicians to identify patients at elevated risk of both ischemic and cognitive complications, facilitating targeted prevention strategies.

The development of comprehensive predictive systems represents a transition toward personalized vascular medicine. Rather than treating all patients with similar degrees of stenosis equally, clinicians can apply individualized risk profiles to determine optimal management. For example, patients with moderate stenosis but low cerebrovascular reserve or elevated hs-CRP levels may require early intervention, whereas those with stable plaques and preserved perfusion can be safely managed conservatively. Such stratification enhances both clinical outcomes and cost-

effectiveness by directing resources to those most likely to benefit from intensive preventive or surgical measures.

This integrated approach has profound implications for public health and healthcare economics. Preventing even a single disabling stroke preserves years of independent living and reduces long-term rehabilitation and social care costs. Protecting cognitive function through early identification of at-risk patients improves quality of life and extends productive lifespan. As the global population ages, predictive vascular–cognitive models offer a sustainable strategy to mitigate the growing burden of cerebrovascular and neurodegenerative disorders.

In conclusion, atherothrombotic carotid disease must be understood as a systemic, dynamic, and neurovascular process rather than a localized mechanical obstruction. Research over the past two decades consistently demonstrates that accurate prediction of ischemic stroke and cognitive decline requires integration of anatomical, hemodynamic, inflammatory, and cognitive parameters. The development and implementation of predictive models that combine these factors represent a major step toward precision prevention in vascular neurology. By uniting advanced imaging, physiological testing, biomarker profiling, and cognitive assessment, clinicians can move beyond traditional risk scoring toward a comprehensive, patient-centered framework that simultaneously reduces stroke incidence, preserves cognitive function, and improves long-term outcomes for individuals with carotid atherothrombosis.

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