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CLINICAL AND NEUROPSYCHOLOGICAL FEATURES OF POST-STROKE COGNITIVE IMPAIRMENT IN DIFFERENT PATHOGENETIC SUBTYPES OF ISCHEMIC STROKE

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Abstract.:

Background: Post-stroke cognitive impairment (PSCI) is one of the most common neurological consequences of ischemic stroke and represents an important cause of long-term functional dependence, reduced quality of life, and impaired social reintegration. The clinical manifestations and severity of PSCI are determined by a complex interaction between the characteristics of the acute ischemic lesion, vascular risk factors, cerebral small vessel disease, stroke severity, lesion location, and premorbid brain reserve. The pathogenetic subtype of ischemic stroke may also influence the pattern and trajectory of cognitive dysfunction.

Objective: To analyze the clinical and neuropsychological characteristics of post-stroke cognitive impairment associated with different pathogenetic subtypes of ischemic stroke and to identify the major factors contributing to the development and persistence of cognitive dysfunction.

Materials and Methods: A comprehensive analysis of contemporary scientific literature concerning post-stroke cognitive impairment, ischemic stroke subtypes, neuropsychological assessment, neuroimaging markers, and cognitive rehabilitation was performed. Particular attention was given to large-artery atherosclerotic, cardioembolic, and small-vessel/lacunar stroke. The Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), executive function tests, memory assessment, attention testing, and neuroimaging were considered as major approaches to the evaluation of PSCI.

Results: Post-stroke cognitive impairment is characterized by substantial heterogeneity. Executive dysfunction, impaired attention, reduced processing speed, memory impairment, and visuospatial deficits are among the most frequently affected domains. Large-artery atherosclerotic stroke is frequently associated with cognitive dysfunction related to cortical or watershed ischemia and chronic cerebral hypoperfusion. Cardioembolic stroke may result in pronounced cognitive impairment because of large cortical and strategically located infarctions and the risk of recurrent embolic events. Small-vessel and lacunar stroke are particularly associated with subcortical executive dysfunction, slowed information processing, and attention deficits, especially in the presence of extensive white matter disease. However, recent longitudinal evidence indicates that long-term cognitive trajectories cannot be explained solely by ischemic stroke subtype, emphasizing the contribution of age, vascular risk factors, cerebral small vessel disease, recurrent stroke, and premorbid cognitive status.

Conclusion: Post-stroke cognitive impairment should be considered a multidimensional consequence of ischemic stroke. Assessment based solely on stroke subtype is insufficient for individual prognosis. A comprehensive approach integrating stroke etiology, lesion location and volume, neuroimaging markers of cerebral small vessel disease, vascular risk factors, and serial neuropsychological assessment may improve early identification of patients at increased risk of persistent cognitive impairment and facilitate personalized rehabilitation.

Keywords: ischemic stroke; post-stroke cognitive impairment; vascular cognitive impairment; cognitive dysfunction; cardioembolic stroke; large artery atherosclerosis; lacunar stroke; cerebral small vessel disease; MoCA; MMSE; neuropsychological assessment.

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1. Introduction. Ischemic stroke remains one of the leading causes of long-term disability worldwide. Although motor, sensory, speech, and visual deficits traditionally receive the greatest attention during the acute and rehabilitation phases, cognitive impairment represents an equally important consequence of cerebrovascular injury. Post-stroke cognitive impairment may interfere with independent living, medication adherence, return to work, communication, rehabilitation participation, and social functioning. The American Heart Association/American Stroke Association recognizes cognitive impairment as a common consequence of stroke with substantial effects on functional independence and quality of life. The clinical spectrum ranges from subtle deficits in individual cognitive domains to major neurocognitive disorder and post-stroke dementia.

Recent systematic evidence suggests that PSCI is common, with pooled prevalence estimates in the range of approximately 39–47%, although the reported frequency varies considerably according to the timing of assessment, diagnostic criteria, patient characteristics, and cognitive instruments used. Importantly, cognitive dysfunction following ischemic stroke does not represent a single homogeneous syndrome. Patients may demonstrate predominant executive dysfunction, memory impairment, attentional deficits, slowed information processing, language disturbance, or visuospatial impairment. In many patients, several cognitive domains are affected simultaneously.

The mechanisms underlying PSCI are also heterogeneous. Acute neuronal injury caused by cerebral ischemia may be accompanied by chronic hypoperfusion, disruption of white matter pathways, blood-brain barrier dysfunction, neuroinflammation, oxidative stress, and secondary neurodegenerative processes. The neurovascular unit and the interaction between vascular and neuronal systems play an important role in maintaining cognitive function.

The pathogenetic subtype of ischemic stroke is therefore of particular interest. According to the TOAST classification, ischemic strokes may be categorized into large-artery atherosclerosis, cardioembolism, small-vessel occlusion, other determined etiology, and undetermined etiology.

2. Pathophysiological mechanisms of post-stroke cognitive impairment

The development of PSCI is determined by several interconnected mechanisms.

2.1. Direct ischemic neuronal injury. Cerebral ischemia results in energy failure, excitotoxicity, calcium dysregulation, mitochondrial dysfunction, oxidative stress, and neuronal death. When ischemic lesions involve cortical and subcortical structures responsible for cognition, clinically significant cognitive dysfunction may develop.

The severity of cognitive impairment depends not only on infarct volume but also on lesion location. Small lesions involving strategically important regions may cause substantial deficits, whereas larger infarcts in less critical areas may produce relatively limited cognitive consequences.

2.2. Disruption of functional brain networks. Cognitive processes depend on distributed neural networks rather than isolated anatomical structures. An ischemic lesion may therefore disrupt remote brain regions through diaschisis and interruption of white matter connections.

Damage to fronto-subcortical circuits may result in impaired executive functions, attention, initiation, cognitive flexibility, and processing speed. Damage to temporal and hippocampal networks may predominantly affect memory.

2.3. Cerebral small vessel disease. Cerebral small vessel disease represents an important contributor to cognitive decline after stroke. White matter hyperintensities, lacunes, cerebral microbleeds, perivascular space abnormalities, and cerebral atrophy may reduce cognitive reserve and increase vulnerability to acute ischemic injury.

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The relationship between vascular pathology and cognition is increasingly understood as a complex interaction between the neurovascular unit, endothelial function, cerebral blood flow, blood-brain barrier integrity, and neuronal metabolism. (Circulation)

2.4. Chronic hypoperfusion. Persistent reduction of cerebral blood flow can compromise neuronal function even in the absence of a new infarction. Chronic hypoperfusion may particularly affect frontal-subcortical circuits and contribute to executive dysfunction and slowed processing speed.

2.5. Neuroinflammation and secondary neurodegeneration. Ischemic stroke induces inflammatory responses involving microglia, astrocytes, cytokines, and other mediators. Persistent inflammatory and vascular processes may contribute to long-term neuronal dysfunction and may interact with pre-existing neurodegenerative pathology.

3. Cognitive profile of different ischemic stroke subtypes

3.1. Large-artery atherosclerotic stroke. Large-artery atherosclerosis is characterized by atherosclerotic disease of major extracranial or intracranial arteries and may result in artery-to-artery embolism, thrombosis, or hemodynamic cerebral ischemia.

Cognitive impairment in this subtype may be associated with: cortical infarction; watershed ischemia; recurrent microembolization; chronic cerebral hypoperfusion; extensive white matter disease; recurrent ischemic events.

Patients may demonstrate impairment of executive functions, attention, processing speed, memory, and language depending on the vascular territory involved.

Atherosclerotic disease may therefore contribute to cognitive decline through both acute focal injury and cumulative vascular damage.

3.2. Cardioembolic stroke

Cardioembolic stroke is commonly associated with atrial fibrillation and other cardiac sources of embolism. Emboli may occlude large cerebral arteries, resulting in extensive cortical or cortico-subcortical infarction.

Cognitive consequences depend primarily on lesion localization and volume. Dominant-hemisphere infarction may produce aphasia and verbal memory impairment, whereas nondominant hemispheric lesions may affect visuospatial processing and attention.

Cardioembolic stroke is also clinically important because of the potential for recurrent embolic events. Repeated cerebral infarctions may progressively reduce cognitive reserve.

The interaction between cardiac disease and brain health is increasingly recognized. Atrial fibrillation, heart failure, and coronary disease may be associated not only with stroke risk but also with structural and functional brain changes relevant to cognition.

3.3. Small-vessel and lacunar stroke. Lacunar infarction results from occlusion of small penetrating arteries and is closely related to cerebral small vessel disease.

Although lacunar infarcts are often relatively small, their cumulative cognitive consequences may be substantial. Lesions involving the thalamus, basal ganglia, internal capsule, corona radiata, or deep white matter may disrupt fronto-subcortical circuits.

The typical cognitive profile includes: reduced processing speed; impaired sustained attention; executive dysfunction; reduced cognitive flexibility; working memory impairment; difficulties with planning and organization.

These deficits may be particularly pronounced when lacunar infarction occurs in the context of extensive white matter hyperintensities and multiple previous lacunes.

Importantly, a recent longitudinal study found that survivors of small-vessel stroke experienced significant declines in global cognition and several cognitive domains over long-term follow-up. However, the investigators did not find a clear difference in overall cognitive trajectory between

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small-vessel stroke and other ischemic stroke subtypes. This finding emphasizes that the relationship between stroke subtype and cognitive outcome is complex rather than deterministic.

3.4. Stroke of other or undetermined etiology. A considerable proportion of ischemic strokes remain cryptogenic or cannot be assigned to a single definitive mechanism. Cognitive outcomes in these patients are heterogeneous.

Undetermined etiology should not automatically be considered equivalent to a benign vascular phenotype. Some patients may have undetected atrial fibrillation, occult small-vessel disease, atherosclerotic plaque, or other vascular mechanisms.

4. Cognitive domains affected after ischemic stroke

4.1. Executive functions. Executive dysfunction is one of the most clinically relevant manifestations of PSCI. Patients may have difficulties with planning, cognitive flexibility, inhibition, problem-solving, and multitasking.

Executive deficits are particularly characteristic of lesions involving frontal-subcortical circuits and are commonly observed in patients with small-vessel disease.

4.2. Attention. Attention may be impaired immediately after stroke and may remain affected during the chronic phase. Patients may experience difficulty maintaining concentration, shifting attention between tasks, and processing simultaneous information.

Attention deficits can significantly interfere with rehabilitation and everyday activities.

4.3. Processing speed. Slowed processing speed is frequently observed after ischemic stroke. Patients may require more time to understand information, formulate responses, or complete routine tasks.

This deficit may be particularly associated with extensive white matter disease and disruption of fronto-subcortical pathways.

4.4. Memory. Memory impairment may involve encoding, storage, retrieval, or working memory. The specific pattern depends on lesion localization and associated vascular pathology.

Hippocampal and medial temporal involvement may result in more prominent episodic memory impairment, whereas subcortical vascular disease may primarily affect retrieval and working memory.

4.5. Language. Language dysfunction is particularly important in patients with dominant-hemisphere cortical infarction. Aphasia may significantly interfere with conventional cognitive testing and can lead to underestimation or misinterpretation of cognitive abilities.

4.6. Visuospatial functions. Visuospatial impairment is more common with right hemispheric and posterior circulation lesions. Deficits may affect navigation, visual construction, spatial orientation, and object perception.

5. Neuropsychological assessment

Early cognitive screening is essential for identifying patients at increased risk of persistent impairment.

The **Montreal Cognitive Assessment (MoCA)** is particularly useful for detecting mild cognitive impairment because it assesses several domains, including executive function, visuospatial abilities, attention, language, memory, and orientation.

The **Mini-Mental State Examination (MMSE)** remains widely used but may be less sensitive to executive dysfunction and mild cognitive impairment.

Additional tests may provide more detailed characterization: Trail Making Test; Digit Span; verbal fluency tests; clock-drawing test; delayed recall tasks; executive function batteries; language assessment; visuospatial testing.

A comprehensive neuropsychological assessment is preferable when the clinical situation allows.

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A recent cohort study demonstrated that visuoconstruction and attention were among the most frequently affected domains, while posterior circulation infarction was associated with impairment across several cognitive domains.

6. Neuroimaging markers associated with cognitive impairment

Magnetic resonance imaging is essential for identifying structural factors associated with PSCI.

Important imaging markers include: infarct volume; infarct localization; cortical involvement; multiple ischemic lesions; white matter hyperintensities; lacunes; cerebral microbleeds; cortical and subcortical atrophy; ventricular enlargement; abnormalities of the hippocampal and temporal structures.

White matter disease is particularly important in patients with small-vessel stroke. Extensive white matter hyperintensities may indicate reduced cerebral reserve and increase vulnerability to subsequent ischemic injury.

The combination of acute infarction and pre-existing vascular brain injury may therefore provide a more accurate explanation of cognitive impairment than infarct size alone.

7. Risk factors for post-stroke cognitive impairment

The development of PSCI is associated with numerous demographic, vascular, clinical, and neuroimaging factors.

Major risk factors include: advanced age; low educational attainment; arterial hypertension; diabetes mellitus; atrial fibrillation; dyslipidemia; smoking; excessive alcohol consumption; coronary artery disease; carotid atherosclerosis; previous stroke; greater neurological severity at admission; cerebral small vessel disease; recurrent stroke.

A systematic review and meta-analysis published in Lancet Neurology identified multiple demographic and vascular factors associated with cognitive impairment and dementia after stroke.

The severity of the initial neurological deficit is also clinically important. Higher NIHSS scores are generally associated with poorer cognitive outcomes.

8. Long-term cognitive trajectories

The course of cognitive function after ischemic stroke is not uniform.

Some patients demonstrate early improvement due to resolution of cerebral edema, restoration of perfusion, and functional reorganization. Others develop persistent impairment or progressive decline.

A large longitudinal analysis published in Stroke in 2025 demonstrated that ischemic stroke survivors experienced significant long-term declines in global cognition, executive function, and memory. Importantly, the study found that cognitive trajectories did not differ substantially between the major ischemic stroke subtypes, suggesting that stroke etiology alone cannot explain long-term cognitive outcomes.

This observation has important clinical implications. Stroke subtype should be regarded as one component of a broader prognostic model rather than an isolated predictor.

The most informative assessment therefore requires serial evaluation at different stages, for example: acute/subacute phase; approximately 3 months; 6 months; 12 months; subsequent annual follow-up in patients with persistent impairment.

9. Relationship between cognitive impairment and recurrent stroke

Cognitive impairment is not only a consequence of stroke but may also be associated with an increased risk of subsequent vascular events.

A 2024 systematic review and meta-analysis including more than 39,000 patients with ischemic stroke found that post-stroke cognitive impairment was associated with a significantly increased risk of recurrent stroke, with a pooled hazard ratio of approximately 1.59.

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Possible explanations include poorer adherence to secondary prevention, impaired ability to manage medications and vascular risk factors, reduced participation in rehabilitation, and a greater underlying burden of cerebrovascular disease.

This creates a potentially important bidirectional relationship between cognitive impairment and recurrent vascular events.

10. Prevention and therapeutic approaches

Management of PSCI should be multidimensional.

The first component is secondary prevention of recurrent stroke, including appropriate management of: arterial blood pressure; diabetes; lipid disorders; atrial fibrillation; smoking; obesity; physical inactivity.

The second component is cognitive rehabilitation. Depending on the patient's cognitive profile, rehabilitation may include attention training, memory strategies, executive-function exercises, compensatory techniques, and structured activities aimed at improving independence.

Physical activity and control of vascular risk factors may also contribute to preservation of brain health.

Pharmacological treatment should be individualized. At present, no single pharmacological strategy can be considered universally effective for all forms of PSCI. The heterogeneity of its mechanisms suggests that future therapeutic approaches should be phenotype- and mechanism-oriented.

11. Clinical implications

The findings reviewed above suggest that assessment of post-stroke cognition should not be limited to a global cognitive score.

A patient with a relatively preserved MMSE may nevertheless have clinically important executive or attentional dysfunction. Therefore, MoCA and domain-specific neuropsychological assessment may provide additional information.

The etiological classification of stroke should be integrated with:

stroke subtype + lesion localization + infarct burden + small-vessel disease + vascular risk factors + baseline cognition + longitudinal cognitive trajectory.

Such an integrated approach may improve prediction of functional outcomes and help identify patients requiring intensified cognitive rehabilitation.

12. Discussion. The relationship between ischemic stroke subtype and cognitive impairment remains an important and incompletely resolved issue.

Theoretical models suggest that cardioembolic and large-artery atherosclerotic strokes may produce more severe cognitive impairment when they cause large cortical or strategically located infarctions. In contrast, small-vessel disease is expected to produce a predominantly subcortical cognitive profile characterized by executive dysfunction, attentional deficits, and slowed processing speed.

However, contemporary longitudinal evidence challenges an overly simplistic subtype-based model. The 2025 Stroke study found significant cognitive decline after ischemic stroke but did not demonstrate major differences in long-term cognitive trajectories among ischemic stroke subtypes.

This apparent discrepancy can be explained by the multifactorial nature of vascular cognitive impairment.

First, patients classified within the same etiological category may have substantially different lesion locations and infarct volumes. Second, vascular risk factors frequently overlap between subtypes. Third, cerebral small vessel disease may coexist with large-artery atherosclerosis or

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cardioembolism. Fourth, pre-existing cognitive impairment may be present before the index stroke and may not be recognized during the acute hospitalization.

Consequently, the pathogenetic subtype should be regarded as an important clinical characteristic but not as an independent determinant of cognitive prognosis.

Another important consideration is the distinction between early post-stroke cognitive impairment and progressive vascular cognitive decline. Some deficits improve during the first months after stroke, whereas others persist or worsen. The trajectory may therefore provide more prognostic information than a single cognitive assessment.

13. Conclusion. Post-stroke cognitive impairment represents a frequent and clinically significant consequence of ischemic stroke. Its manifestations range from isolated impairment of attention or processing speed to multidomain cognitive dysfunction and major neurocognitive disorder.

Different pathogenetic subtypes of ischemic stroke may be associated with distinct mechanisms and cognitive profiles. Large-artery atherosclerotic stroke may be accompanied by cortical, watershed, and hypoperfusion-related cognitive dysfunction; cardioembolic stroke may produce substantial deficits following large or strategically located cortical infarctions; and small-vessel/lacunar stroke is frequently associated with executive, attentional, and processing-speed deficits related to disruption of subcortical networks.

Nevertheless, contemporary evidence indicates that long-term cognitive trajectories cannot be predicted solely from stroke etiology. Age, education, stroke severity, lesion location and volume, recurrent cerebrovascular events, vascular risk factors, cerebral small vessel disease, and premorbid cognitive reserve must also be considered. (PubMed)

Therefore, comprehensive and repeated neuropsychological assessment should become an integral component of post-stroke care. The combination of etiological classification, neuroimaging, standardized cognitive testing, vascular risk-factor management, and individualized cognitive rehabilitation represents the most rational strategy for improving long-term outcomes.

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