COGNITIVE IMPAIRMENT FOLLOWING ISCHEMIC AND HEMORRHAGIC STROKE

A SCIENTIFIC STATEMENT FROM THE AMERICAN HEART ASSOCIATION/AMERICAN STROKE ASSOCIATION

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DEFINITIONS
• **Vascular cognitive impairment (VCI):** cognitive impairment of any severity associated with cerebrovascular disease irrespective of the occurrence of stroke symptoms.
  • Vascular injuries leading to VCI include insidious, progressive microvascular changes (i.e. diffuse white matter injury, cerebral microbleeds, enlarged perivascular spaces, cortical microinfarcts) as well as single or multiple clinical stroke events impacting brain structures critical for cognition

• **Vascular dementia (VaD):** end of a continuum of severity of clinical manifestations of VCI

• **Post-stroke cognitive impairment (PSCI):** any severity of cognitive impairment, irrespective of cause, noted after an overt stroke

• **Post-stroke dementia (PSD):** end of a continuum of severity of clinical manifestations of PSCI and refers to all types of dementia after stroke

• **ICH:** intracerebral hemorrhage

• **AIS:** acute ischemic stroke

• **SAH:** Subarachnoid hemorrhage
PSCI: PREVALENCE AND INCIDENCE

- Substantial heterogeneity in reporting
- Impacted by multiple factors (timing of assessment, diagnostic criteria, demographics, etc.)
- Most common in first year after stroke
  - 60% cumulative incidence in first year
  - Highest rate right after stroke
  - Pooled prevalence of PSCI without dementia 38%
- Even if not meeting criteria for dementia, PSCI impacts quality of life
- Rates can be impacted by preexisting cognitive impairment
PSD : PREVALENCE AND INCIDENCE

• Less frequent than milder forms of cognitive impairment after stroke
• Varies by stroke severity and recurrent stroke history
• Rates in first year 7.4% (first stroke, pre-stroke dementia excluded)-41.3% (recurrent stroke, pre-stroke dementia included)
• Overall estimates:
  • 10% have dementia before first stroke
  • 10% after first stroke
  • 1/3 after recurrent stroke
RACIAL DISPARITIES

• Differences in frequency and severity of PSCI reported
  • Black patients have greater cognitive decline and more frequent post-stroke dementia within 5 years of ischemic stroke than White patients
  • This occurs despite Black patients having younger age at time of incident stroke
PSCI AND PSD: ICH

• Frequent in patients with ICH
  • Higher in patients with lobar ICH

• New-onset dementia 14.2% 1 year after ICH
  • Lobar ICH 23.4% vs non-lobar ICH 9.2%

• New-onset dementia 28.3% at 4 years
SAH AND COGNITION

• Common to have impairment in at least one neuropsychological domain
• Global mental status impairment 3 months after SAH 26-43%
  • 21% at 1 year
PSCI NATURAL HISTORY
NATURAL HISTORY

• Variable, can:
  • Start at stroke onset and stabilize
  • Start at stroke onset and progress
  • Develop after recurrent strokes
  • Develop at onset of stroke in presence of pre-existing cognitive impairment
  • Develop more than 3-6 months after stroke
• Estimates of impairment early in course may overestimate as improvement may occur
• Long-term data on PSCI limited
DELAYED ONSET PSCI

• PSCI >3-6 months after stroke
  • Overall incidence of new dementia >1 year after stroke 1.7% per year
    • varies by stroke severity
• Risks differ from early PSCI
  • Recurrent stroke
  • Progression of small vessel disease/covert stroke
  • Older age
  • Baseline cognitive impairment
  • Hypertension
  • Diabetes
  • Brain atrophy
DIFFERENTIAL DIAGNOSIS
EVALUATION OF DECLINE IN COGNITIVE FUNCTION POST-STROKE

- Cognitive function post-stroke can be impaired by other complications, pre-stroke cognitive decline, and co-existing age-related neuropathologies
- Delirium a common complication of stroke and should be differentiated from PSCI
- Assess patients for delirium and for causes of delirium (medications, infection, pain, etc.)
- Exclude reversible causes of cognitive impairment
- TSH, vitamin B12
- assess for mood disorders, hearing or vision impairments, sleep disorders, sedating and anticholinergic medications
ASSESSMENT OF COGNITIVE FUNCTION POST-STROKE

• Differentiate pre-stroke cognitive decline from post-stroke cognitive decline
• Can be assessed by patient and informant questioning
  • Cognitive-related activities of daily living or validated questionnaires
• Common to have multiple etiologies of dementia
  • More research needed on how to diagnose underlying neurodegenerative pathologies in the setting of recent stroke
SYMPTOMS & COGNITIVE DOMAINS AFFECTED
STROKE LOCATION & COGNITION

• Location linked to type of deficits but not perfectly predictive of cognitive impairment

• Locations associated with increased risk of PSCI:
  • Left frontotemporal, left angular gyrus, left basal ganglia structures and surrounding white matter, left thalamus, right parietal lobe, left middle cerebral artery territory

• Given overlap of these regions and aphasia and cognitive screening dependence on language, severity of cognitive impairment may be overestimated in patients with aphasia
COGNITIVE DOMAINS

• Executive function and attention difficulty common
  • Reported to show most improvement by 3-6 months
• Language does not tend to improve
• Global deficits described but may reflect use of global measures
• Deficits similar between ICH and AIS patients
• Executive function and verbal memory most affected in SAH
PATHOPHYSIOLOGY
PATHOPHYSIOLOGY

- Small vessel disease biggest contributor to VCID
- PSCI pathophysiology less well understood
  - Likely brain reserve and resilience play a role in degree of cognitive impairment

**Brain reserve:** difference between degree of brain damage observed and clinical manifestation of that damage

**Brain resilience:** brain’s capacity to counteract accumulated damage combined with compensatory mechanisms that can be used to mitigate effects
BRAIN HEALTH & THE NEUROVASCULAR UNIT

• Brain health: brain’s capacity to operate at its optimal state

• Neurovascular unit is the key structural element
  • Often damaged by stroke
  • Damage possibly leads to PSCI
  • Possible points of intervention for future treatment & prevention

Neurovascular Unit

• Neurons
• Astrocytes
• Pericytes
• Microglia
• Blood vessels
PSCI RISK FACTORS
RISK FACTORS & VULNERABILITY FACTORS

RISK FACTORS
• Pre-stroke cognitive decline
• Pre-existing cerebral vulnerability/reduced reserve
• Stroke impact

VULNERABILITY
• Pre-existing reduced brain reserve
• Risks factors for increased vulnerability: age, small vessel disease, neurodegeneration
OTHER ASSOCIATIONS

• PSCI frequently co-exists with post-stroke depression
• Strong social networks may be protective, though data sparse
• More common with higher stroke burden
  • Brain imaging can serve as a proxy, though extent of ability to predict unclear
• Rates higher in ICH, specifically lobar ICH
  • Likely related to underlying cerebral amyloid angiopathy
  • In SAH, linked to delayed cerebral ischemia and chronic hydrocephalus
• Post-stroke delirium associated with higher rates of post-stroke dementia
ASSOCIATION WITH OTHER POST-STROKE OUTCOMES
OTHER POST-STROKE OUTCOME ASSOCIATIONS

• Associated with other common post-stroke outcomes that contribute to lower quality of life
  • Physical disability, sleep disorders, depression, neuropsychological changes
  • These comorbidities can complicate or delay diagnosis
• Assessment of functional outcomes (mRS, Barthel, ADL assessments) are affected by cognitive impairment
• Poor cognition may impact participation in rehabilitation
• Along with cognition, patients should be assessed for these other conditions
• Improved physical activity and antidepressant use may benefit cognition, though minimal clinical trial data
Reduced quality of life

Mood disorder with depressive features, major depressive-like episode, or mixed-mood features

Depression (30-35%)

Poststroke cognitive impairment (22-80%)

Poststroke dementia (7-41%)

The lack of ability to perform a task or activities of daily life in the range considered normal for an individual

Physical/functional disability (40-60%)

Feelings of early exhaustion, weariness, lack of energy and aversion to effort not ameliorated by rest

Fatigue (45-55%)

Conditions that disturb normal sleep, e.g., insomnia, sleep disordered breathing and restless legs syndrome

Sleep disorders (50-60%)

Presence of multiple (>2) co-occurring health conditions, adding complexity to disease management

Multimorbidity (>40%)

Multidimensional syndrome of diminished goal-directed behavior, emotion, and cognition

Apathy (30-40%)

Excessive or chronic feelings of tension, extreme apprehension and worry

Anxiety (20-25%)
SCREENING AND DIAGNOSTIC MODALITIES
SCREENING FOR PSCI

• Cognitive complaints are common
• Who to screen, when, and how often not clear
  • Need to screen if complaints or clinical concerns
• Informant report is insensitive to PSCI
• Objective assessment is critical
• No gold standard for cognitive screening post-stroke
• Early detection in acute setting essential for early planning and treatment
  • Reassessment important
SCREENING TESTS

• Several brief tests have been used
  • Mini-Mental State Examination (MMSE)
  • Montreal Cognitive Assessment (MoCA)
    • Generally recommended, more sensitive to mild impairment, less ceiling effect
• Most screens not developed for heterogeneous presentations of PSCI
• Stroke deficits and individual patient factors (demographics, cultural, linguistic) may limit utility of standard tools
MANAGEMENT OF POST-STROKE COGNITIVE IMPAIRMENT
INTERDISCIPLINARY COLLABORATION

- Neurologists, gerontologists and PCPs can enlist many allied health professionals in post-stroke evaluation
- Examples include: SLP, OT, Neuro-Psych, RNs
- Not all patients will need all modalities – tailor the team to each individual patient
- Telehealth can assist with monitoring and management of cognitive deficits

CARE PARADIGM

1. Do results from the cognitive screening test indicate possible cognitive impairment?
   - YES: Refer for neuropsychological evaluation
   - NO: Further cognitive evaluation is probably not warranted at this time

2. Is there evidence of cognitive impairment?
   - YES: Is there evidence that cognitive impairment impact daily functioning?
     - YES: Refer to appropriate professional (e.g., Occupational Therapy)
     - NO: Refer to appropriate health professional (e.g., Speech Language Pathology)
   - NO: Does patient or informant report cognitive decline?
     - NO: Is there evidence of limited awareness of cognitive deficits in the patient?
       - NO: Is there evidence of communication deficits?
         - YES: Refer to appropriate health professional (e.g., Speech Language Pathology)
         - NO: Refer to appropriate professional (e.g., Occupational Therapy)
MANAGEMENT PEARLS – POST STROKE COGNITIVE IMPAIRMENT

COGNITIVE REHABILITATION
• Small gains in multiple domains identified in literature review
  • Memory, executive functioning and neglect
  • Attention training has inconsistent benefits
• Virtual tools may be beneficial for cognitive rehab
  • Patient’s own device – gamified tools
  • Caregiver training and education

PHYSICAL ACTIVITY
• Small studies suggest aerobic activity may improve cognitive function
• Tai Chi, boxing and resistance training studied in small sample sizes
• Virtual tools (e.g. Wii Fit, Oculus Rift) have inconclusive evidence
MANAGEMENT PEARLS – POST STROKE COGNITIVE IMPAIRMENT

MEDICAL MANAGEMENT
• Secondary Stroke prevention is paramount
  • Risk of PSCI increases with subsequent strokes
• BP control is associated with lower risk of dementia in general population
  • Also associated with lower risk of primary and secondary strokes
• Integrated vascular risk factor modification has been effective in slowing progression of AD
  • Further research needed to establish impact in PSCI
• Reduction in final lesion size via acute stroke intervention may reduce risk of PSCI
  • Improved functional and cognitive outcomes among EVT and thrombolysis recipients c/w no treatment
• No consistent benefits of SSRIs or dopamine agonists following stroke
• Studies of cholinesterase inhibitors and memantine have shown small positive effect in
  • complicated by high rates of adverse events and patient discontinuation

COMPLIMENTARY AND INTEGRATIVE TREATMENTS
• Transcranial magnetic stimulation (TMS) shows small improvement in cognitive and attention performance
• Other modalities plagued by poor quality studies
  • Acupuncture
  • Neuromodulation
  • Herbal supplements & vitamins
  • DASH and Mediterranean diets
ANTICIPATORY GUIDANCE – FOR CLINICIANS

WHEN COGNITIVE IMPAIRMENT DETECTED
- Characterize affected domains
- Assess for safety issues
- Connect with Community Resources
- Address Caregiver Fatigue
- Introduce Advanced care planning tools

HOME SAFETY CONCERNS
- Toileting
  - Grab bars, raised toilet seats
- Mobility and Communication
  - Provide mobility tools
  - Simplify access to emergency help
- Transitional Care processes increase home safety
  - Reduce Falls
  - Reduce readmissions
ANTICIPATORY GUIDANCE – FOR CLINICIANS

RETURN TO WORK
• Cognitive decline risk higher in those who do NOT return to work or those who were unemployed before stroke
• Cognitive/vocational rehab can assist
• Lack of knowledge of invisible deficits hinders return to work and staying employed

DRIVING
• Common source of pride and independence
• 1/3 of stroke patients require training or rehab before resuming driving
• Attention and executive functioning performance linked to resuming driving
• Limited data supporting any particular intervention to improve performance
SUMMARY

Cognitive and brain reserve
- Educational or occupational attainment
- Genetic factors
- Neuroanatomical and structural properties of the brain
- Functional properties of the brain

Risk factors for PSCI
- Older age
- Cardiovascular disease
- "Strokes" stroke location
- Stroke severity
- Pre-existing cognitive impairment
- Vascular comorbidities
- Stroke recurrence
- Co-existing neurodegenerative disease
- Diabetes

Pathophysiology of PSCI
- Pre-existing brain pathology (neurovascular, neurodegenerative)
- Loss of structural and functional connectivity
- Disruption of the neurovascular unit

Assess for cognitive impairment:
- Objective cognitive assessment using bedside screening tools and/or formal neuropsychological testing

Explore and manage alternative diagnoses:
- Delirium
- Depression
- Metabolic disturbance
- Infections
- Medication side effects and polypharmacy
- Hearing and/or vision impairments
- Pre-stroke cognitive decline

Management of Post-Stroke Cognitive Impairment

- Manage associated comorbidities
  - Physical disability
  - Sleep disorders
  - Social isolation
  - Mood and anxiety disorders

- Anticipatory Guidance
  - Home safety
  - Driving safety
  - Return to work
  - Support for caregivers
  - Caregiver fatigue

- Minimize progression of cognitive impairment
  - Secondary stroke prevention

- Optimize functioning
  - Cognitive rehabilitation and interdisciplinary care
  - Neuropsychology, speech and occupational therapy
  - Physical activity
  - Consider pharmacological treatments
SUMMARY & FUTURE DIRECTIONS

MULTIPLE AREAS OF FUTURE INVESTIGATION
• Mechanisms of PSCI
• Stroke subtypes, preexisting pathology
• Social/cultural factors
• Cognitive Screening
• Need for adequately powered trials of rehab, lifestyle modification, and pharmaceuticals
• Further study of multidisciplinary clinics & other care models

DISCOVERY STUDY (DETERMINANTS OF INCIDENT STROKE COGNITIVE OUTCOMES AND VASCULAR EFFECTS ON RECOVERY)
• 8,000 patient multicenter study of ischemic and hemorrhagic stroke patients
• Patients with no dementia history enrolled and followed for 2 years
• Serial cognitive and functional assessments, MRI, PET imaging, genetics and biomarker tests