Cognitive Effects After Carotid Intervention: Can Patients Actually Have Improved Function?

Wei Zhou, MD
Professor and Chief, Division of Vascular Surgery
University of Arizona
Banner University Medical Center
Disclosures

- Grant funding
  - AHA: CRP
  - NIH NINDS
    - NIH R01: Cognitive effect of microemboli following CAS
    - NIH R21: Neuroimaging correlates of memory decline following carotid interventions
Cognition
- “A Problem for Our Age”
Higher silence infarcts, larger white matter hyper-intensity, poorer executive function

CVH Study: Cognitive impairment and decline

Perform worse on cognitive measures
Perfusion

Cerebral Perfusion is Associated with White Matter Hyperintensities in Older Adults with Heart Failure

Michael L. Alosco, B.A.1, Adam M. Brickman, Ph.D.2, Mary Beth Spitznagel, Ph.D.3, Sarah L. Garcia, B.A.4, Atul Narshede, M.S.5, Erica Y. Griffith, B.S.6, Naftali Raz, Ph.D.4, Ronald Cohen, Ph.D.5, Lawrence H. Sweet, Ph.D.6, Lisa H. Colbert, Ph.D.7, Richard Josephson, M.S., M.D.8,9,10, Joel Hughes, Ph.D.1,3, Jim Rosneck, M.S.3, and John Gunstad, Ph.D.1,3

1Department of Psychology, Kent State University, Kent, OH 2Taub Institute for Research on Alzheimer’s Disease and the Aging Brain, Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY 3Department of Psychiatry, Summa Health System, Akron City Hospital, Akron, OH 4Institute of Gerontology, Wayne State University, Detroit, MI 5Departments of Neurology Psychiatry and the Institute on Aging, Center for Cognitive Aging and Memory, University of Florida 6Department of Psychology, University of Georgia, Atlanta, USA 7Department of Kinesiology, University of Wisconsin, Madison, WI 8University Hospitals Case Medical Center and Department of Medicine, Cleveland 9Harrington Heart & Vascular Institute, Cleveland, OH 10Case Western Reserve University School of Medicine, Cleveland, OH

Abstract

Cognitive impairment is common in heart failure (HF) and believed to be the result of cerebral hypoperfusion and subsequent brain changes including white matter hyperintensities (WMH). The current study examined the association between cerebral blood flow and WMH in HF patients and the relationship of WMH to cognitive impairment. Sixty-nine patients with HF completed the mini mental state examination (MMSE), echocardiogram, transcranial Doppler sonography (TCD) for cerebral blood flow velocity of the middle cerebral artery and brain magnetic resonance imaging (MRI). Multivariable hierarchical regression analyses controlling for medical and demographic characteristics as well as intracranial volume showed reduced cerebral blood flow velocity of the middle cerebral artery was associated with greater WMH (β = -34, p = .02). Follow up regression analyses adjusting for the same medical and demographic factors in addition to cerebral perfusion also revealed marginal significance between increased WMH and poorer performance on the MMSE (β = -26, p = .05). This study suggests that reduced cerebral perfusion is associated with greater WMH in older adults with HF. Our findings support the widely proposed mechanism of cognitive impairment in HF patients and prospective studies are needed to confirm our findings.
16.5% had embolic signals at baseline

> 40% of asymptomatic lesions have embolic signal during a follow-up of 4 years

Best medical therapy improves baseline microemboli 12.6% → 3.7%
Cerebral microemboli and cognitive impairment

David Russell

Department of Neurology, University of Oslo, Rikshospitalet, 0027, Oslo, Norway

Abstract

Transcranial Doppler Ultrasound (TCD) may be used to detect cerebral microemboli in patient groups with an increased stroke risk and during invasive cardiovascular examinations and operations. Although these microemboli do not cause immediate symptoms, there is growing evidence which suggests that they may cause cognitive impairment if they enter the cerebral circulation in significant numbers. This has been studied in detail in patients who have had coronary artery bypass surgery. In these patients, an association has been found between the number of intraoperative cerebral microemboli detected by transcranial Doppler and postoperative neuropsychological outcome.

It is also possible that cerebral microemboli may be the cause of cognitive impairment in patients with cerebrovascular disease. Cerebral microemboli are often found in patients with atherosclerosis, especially of the carotid arteries and aortic arch, and in patients with heart disease. There is also an increased risk for silent strokes and cognitive impairment in these patients.

Prospective clinical studies are therefore required to determine if continuous cerebral microembolization to the brain will lead to progressive cognitive impairment.

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Carotid Revascularization and Cognition
Surgical Revascularization Reverses Cerebral Cortical Thinning in Patients With Severe Cerebrovascular Steno-Occlusive Disease

Jorn Fierstra, MSc; David B. MacLean, BSc; Joseph A. Fisher, MD; Jay S. Han, MSc; Daniel M. Mandell, MD; John Conklin, MSc; Julien Poublanc, MSc; Adrian P. Crawley, PhD; Luca Regli, MD; David J. Mikulis, MD; Michael Tymianski, MD, PhD

- Stroke 2011
Carotid Interventions

Memory Changes

Improved

MMSE Changes

Declined

26%

39%
Procedure-related Embolization

- **Subclinical microembolization**
  - common (25-70%), 3x more following carotid stenting than carotid endarterectomy
  - Not associated w/neurologic symptoms
## Table I: Neuropsychological tests to evaluate cognitive function

<table>
<thead>
<tr>
<th>Cognitive domains</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individual Difference/General Screen</strong></td>
<td></td>
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<tr>
<td>IQ estimate</td>
<td>WTAR</td>
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<tr>
<td>General Functioning</td>
<td>MMSE</td>
</tr>
<tr>
<td>Depression</td>
<td>GDS (15 item)</td>
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<tr>
<td><strong>Attention/Executive/Speed</strong></td>
<td></td>
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<tr>
<td>Psychomotor speed</td>
<td>Digit Symbol subtest (WAIS-III)</td>
</tr>
<tr>
<td>Psychomotor speed</td>
<td>Trail Making Test (Part A)</td>
</tr>
<tr>
<td>Executive</td>
<td>Trail Making Test (Part B)</td>
</tr>
<tr>
<td>Attention/Working Memory</td>
<td>Digit Span subtest (WMS-III)</td>
</tr>
<tr>
<td>Attention/Working Memory/Executive</td>
<td>Letter/Number Span (WMS-III)</td>
</tr>
<tr>
<td><strong>Motor speed and strength</strong></td>
<td></td>
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<tr>
<td></td>
<td>Grooved Pegboard Task</td>
</tr>
<tr>
<td><strong>Memory</strong></td>
<td></td>
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<tr>
<td>Verbal</td>
<td>Logical Memory subtest (WMS-III)</td>
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<tr>
<td>Verbal</td>
<td>RAVLT</td>
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<tr>
<td>Visual</td>
<td>Faces subtest (WMS-III)</td>
</tr>
<tr>
<td><strong>Visuospatial Function</strong></td>
<td></td>
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<td></td>
<td>Clock Drawing</td>
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<tr>
<td><strong>Language</strong></td>
<td></td>
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<tr>
<td>Executive/language</td>
<td>Category Fluency</td>
</tr>
<tr>
<td>Confrontation Naming</td>
<td>Boston Naming Test (CERAD 15 item)</td>
</tr>
</tbody>
</table>

Regions implicated in executive control, mental speed, and memory
- Rosen.Zhou et al, Neuroimage: Clinical, 2018
Prospective neurocognitive evaluation of patients undergoing carotid interventions

Wei Zhou, MD, Elizabeth Hitchner, MA, Kathleen Gillis, RNP, Lixian Sun, MS, Rebecca Floyd, BS, Barton Lane, MD, and Allyson Rosen, PhD, Palo Alto and Stanford, Calif

Microembolization is associated with transient cognitive decline in patients undergoing carotid interventions

Elizabeth Hitchner, MA, Brittanie D. Baughman, MS, MBA, Salil Soman, MD, Becky Long, BS, Allyson Rosen, PhD, and Wei Zhou, MD, Palo Alto and Stanford, Calif, and Cambridge, Mass

Decline @ 1 mo, recovered @ 6 mo

Δ Score

Microemboli correlate with memory (RAVLT) decline at one month postop

Improvement

No emboli N=35

With Emboli N=45

p = 0.05
Volumetric Distribution of Emboli (CEA and CAS)
CEA vs. CAS

**Verbal Learning Memory Changes**

- **RAVLTsum Changes**
  - **CEA**
  - **CAS**

<table>
<thead>
<tr>
<th></th>
<th>1-mo postop</th>
<th>6-mo postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAS</td>
<td></td>
<td></td>
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</tbody>
</table>
Volume of subclinical embolic infarct correlates to long-term cognitive changes after carotid revascularization

Wei Zhou, MD, Britannie D. Baughman, MS, Salil Soman, MD, Max Wintermark, MD, Laura C. Lazzeroni, PhD, Elizabeth Hitchner, MS, Jyoti Bhat, MS, and Allyson Rosen, PhD, of Palo Alto and Stanford, Calif, and Cambridge, Mass

Mean Memory Change at 6 Mos in CAS Cohort

Embolic Vol<100mm3
100-500mm3
>500mm3

RAVLTsum
RAVLT-SD
RAVLT-LD
Baseline Brain Organization

Brain Structural Connectivity Distinguishes Patients at Risk for Cognitive Decline After Carotid Interventions

Salil Soman, Gautam Prasad, Elizabeth Hitchner, Payam Massaband, Michael E. Moseley, Wei Zhou, and Allyson C. Rosen

Soman et al, Human Brain Mapping 37: 2185-94
A Prospective Evaluation of Systemic Biomarkers and Cognitive Function Associated With Carotid Revascularization

Mary C. Zuniga, BS,* Thuy B. Tran, MD,† Brittanie D. Baughman, MS, MBA,* Gayatri Raghuraman, PhD,* Elizabeth Hitchner, MS,* Allyson Rosen, PhD,* † and Wei Zhou, MD* †

### TABLE 4. Predictors of significant Cognitive Decline at 6 Months After Carotid Revascularization

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDF-1α</td>
<td>1.00001</td>
<td>1.00004–1.0002</td>
<td>0.004</td>
</tr>
<tr>
<td>TNF-α</td>
<td>1.06</td>
<td>1.02–1.10</td>
<td>0.006</td>
</tr>
<tr>
<td>CAS</td>
<td>6.50</td>
<td>1.04–31.28</td>
<td>0.020</td>
</tr>
<tr>
<td>Age &gt; 80 yrs</td>
<td>12.71</td>
<td>1.43–112.87</td>
<td>0.023</td>
</tr>
<tr>
<td>Preop RAVLT sum</td>
<td>4.36</td>
<td>0.87–21.73</td>
<td>0.073</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.97</td>
<td>0.95–0.99</td>
<td>0.019</td>
</tr>
</tbody>
</table>
Summary

- Carotid disease affects cognition
- Carotid intervention may have a positive or negative effect on cognition. Need to select right therapy for right lesion